Effect of a Nano-Hydroxyapatite Paste on Bleaching-Related Tooth Sensitivity

WILLIAM D. BROWNING, DDS, MS*, **SOPANIS D. CHO,** DDS, MSD†, **EDWARD J. DESCHEPPER,** MAED, DDS, MSD‡

ABSTRACT

Statement of the Problem: Bleaching-related tooth sensitivity has been shown to be facilitated by the presence of enamel defects. A nano-hydroxyapatite (n-HAP) paste has been shown to repair these defects.

Purpose of the Study: Using a randomized clinical trial, an n-HAP paste was investigated to determine its efficacy in reducing bleaching-related tooth sensitivity.

Methods and Materials: An n-HAP paste (Renamel AfterBleach®, Sangi Co., Ltd., Tokyo, Japan) and a placebo (zero-HAP) were randomly assigned for use in 42 participants. A 7% hydrogen peroxide gel was used twice daily for 14 days, with use of assigned desensitizer for 5 minutes immediately following. A diary was completed daily for 4 weeks to note: use of the agents and sensitivity on a visual analog scale (VAS). Three aspects of tooth sensitivity were investigated: percentage of participants; number of days; and intensity level. Color change was assessed.

Results: For Groups zero-HAP and n-HAP, respectively, 51 and 29% of participants reported tooth sensitivity ($p = 0.06$). Days of sensitivity were 76 and 36, respectively ($p = 0.001$). Change in VAS score from baseline trended higher for Group zero-HAP ($p = 0.16$). Color change was equivalent.

Discussion: The data trend indicated Group n-HAP experienced less sensitivity over all three measures. Only the number of days of sensitivity was statistically significant.

Conclusion: Within the limits of the study it can be concluded that the use of the n-HAP paste was associated with a statistically significant reduction in the number of days of tooth sensitivity experienced during active bleaching.

CLINICAL RELEVANCE

For those using a tooth whitener without a desensitizing agent, this study indicates that a paste containing nano-hydroxyapatite crystal can effectively reduce the duration of tooth sensitivity.

(J Esthet Restor Dent 24:268–276, 2012)

INTRODUCTION

Historically three measures of tooth sensitivity during tooth bleaching have been used. Each is a self report of pain participants experienced in going about their daily activities. Studies have reported the percentage of participants who experienced sensitivity.[1–4] This measure provides practitioners with an estimate of the likelihood that their patients will experience tooth sensitivity during bleaching. A second approach has

*Professor and IDA Endowed Chair In Restorative, Restorative Department, Indiana University School of Dentistry, 1121 West Michigan Street, Indianapolis, IN 46202, USA

†Assistant Professor, Restorative Department, Indiana University School of Dentistry, 1121 West Michigan Street, Indianapolis, IN 46202, USA

‡Professor and Division Head of Operative Dentistry, Restorative Department, Indiana University School of Dentistry, 1121 West Michigan Street, Indianapolis, IN 46202, USA

 DOI 10.1111/j.1708-8240.2011.00437.x © 2011 Wiley Periodicals, Inc.

been to measure the proportion of days spent actively bleaching, which result in tooth sensitivity.[5–7] This measure provides practitioners with an estimate as to duration of sensitivity. A third approach has been to have patients assess their level of pain from daily activities during bleaching using a visual analog scale (VAS)[8] or similar pain rating scale.[9,10] This measure provides practitioners with an estimate of the intensity of pain their patients may experience.

Each measure investigates a different aspect of tooth sensitivity; each has value. For any given study, the decision to use two, three, or more measures adds to the complexity. The time investment and the number of required subjects increase. In short, additional complexity requires additional resources—resources that are scarce. Accordingly studies tend to report only one or two measures of sensitivity. The present study investigated all three aspects of tooth sensitivity.

Many commercially available whitening agents contain agents intended to reduce tooth sensitivity. Some have been shown to be effective.[11] Direct-to-consumer whitening agents, by contrast, generally do not contain desensitizers. The present study investigates a desensitizing agent that follows application of the tooth whitener and is used as a separate step. If shown to be effective, this agent would be of benefit to people using a whitener that does not contain a desensitizing agent.

Tooth sensitivity during whitening has been associated with microscopic surface defects and sub-surface pores in enamel. It has been theorized that these defects allow rapid ingress of the whitening agent to the pulp and this results in sensitivity. In theory, a product that encourages repair of these microscopic defects can reduce sensitivity.[12]

These defects reflect changes of the crystalline structure of enamel or the hydroxyapatite. Laboratory studies have shown these microscopic pores can be repaired using a paste containing nano-sized hydroxyapatite (n-HAP) crystals.[13–15] Some additional support is offered by anecdotal clinical reports that n-HAP is an effective desensitizer. However, these provide only low-level evidence. These are best used as preliminary investigation only, as their relevance to clinical practice is unknown. The present study will provide higher level evidence regarding the efficacy of n-HAP.

The purpose of this study was to investigate the potential for these crystals to reduce tooth sensitivity. The study investigates the three measures of sensitivity described earlier via a formal clinical trial. Two groups were created. The treatment group used a paste containing n-HAP crystals daily whereas the control group used a placebo.

Concerning comparisons between the two groups during active bleaching, there were three study hypotheses. First, the treatment group would have a lower percentage of participants reporting tooth sensitivity. Second, the treatment group would experience fewer days of tooth sensitivity. Third, the average change in sensitivity scores related to normal daily activities would be lower for the treatment group. The null hypothesis in each comparison was there would be no significant difference between groups.

Evaluations were also made to assess the change in color from baseline. These are presented as additional observations to assess the efficacy of a tooth whitener when used in conjunction with a separate desensitizing agent.

MATERIALS AND METHODS

The study was conducted as a randomized, placebo-controlled, parallel group, double-blind clinical trial. Two "desensitizing" agents, identified in this report as zero-HAP and n-HAP, were compared. The desensitizer was applied in a separate step immediately following bleaching. Paste n-HAP was Renamel AfterBleach® (Sangi Co., Ltd., Tokyo, Japan), which contained n-HAP crystals. Paste zero-HAP, the placebo, was identical with the exception that it did not contain the nano-sized particles of hydroxyapatite. Thus, Group zero-HAP was the control group and Group n-HAP the treatment group.

© 2011 Wiley Periodicals, Inc. *DOI 10.1111/j.1708-8240.2011.00437.x*

All participants in the study were adults in good general health with maxillary incisor teeth equal to or darker than shade LV A2 on the Vita Classical shade guide. All potential participants were examined to assure that the health of their dentition and oral soft tissues were within the normal range. All potential subjects were informed and gave their written consent to participate. The study protocol and the informed consent document were approved by the university's Institutional Review Board.

Forty-two participants were enrolled, 21 in each group. Each person had his/her maxillary teeth polished. For each participant a polyvinylsiloxane impression of the maxillary teeth was made, and an improved stone model fabricated from the impression. From this model a soft stent (SofTray, Ultradent Products, Inc., South Jordan, UT, USA) was fabricated with 0.5 mm of labial block-out. The margin of the stent was extended onto the attached gingiva. Stents were evaluated for fit and adjusted as needed at the baseline appointment.

Due to concerns about introducing a confounding factor into the study, all participants were warned against using any oral health care products that contained a desensitizer. Participants were provided fluoride toothpaste without any desensitizing agents to use throughout the study (Aim Ultra Mint Gel toothpaste, Church & Dwight Co., Inc., Princeton, NJ, USA). The bleaching agent used by all participants was a 7% hydrogen peroxide product. This concentration of hydrogen peroxide correlates to approximately 24% carbamide peroxide. Again, to avoid introducing a confounding factor, the bleaching agent was compounded by a licensed pharmacist (Table 1). It did not contain a desensitizer.

Participants used the whitening agent twice daily for 2 weeks. They wore the bleaching agent for 30 minutes. Whereas use of a higher concentration of active ingredient and use of whitener on multiple occasions per day have been associated with increased sensitivity levels,[4,16] shorter application time correlates to reduced sensitivity. As a result we anticipated participants would experience normal sensitivity levels. Participants used their assigned desensitizing agent during the 2 weeks of active bleaching and for 1 week after the end of active bleaching. Participants were free to choose bleaching times that were convenient to them, but were encouraged to separate the twice daily applications of the whitening agent and desensitizer by at least 1 hour. During the week following bleaching participants were similarly free to choose a convenient time for the twice daily application of the desensitizer.

TABLE 1. Ingredients

Hydrogen peroxide, 30% ACS
Saccharin sodium
Polysorbate 20 NF
Sorbital solution USP 70%
Menthol Crystals USP Natural
Flavor, methyl salicylate NF syn. Wintergreen
Ethyl alcohol USP 190 proof USP
Pluronic F127 gel
All ingredients were pharmaceutical grade and were compounded to create a 7% hydrogen peroxide whitening gel.

Participants were randomly assigned to use desensitizing agent zero-HAP or n-HAP according to a preset randomization chart. Participants and evaluators were unaware of which group represented the treatment group until after the completion of the study. Evaluators provided verbal and written instructions and demonstrated how to use the stent and all study products. Participants were instructed to fill the stent using the minimum amount of whitening agent required to adequately fill the tray, about one-third syringe, and wear it for 30 minutes. They were further instructed to then clean the tray of any residual bleaching agent. Next they were to place a generous amount, about one-half a syringe, of the desensitizing agent in the tray and wear it for 5 minutes. Following this application, they were instructed to clean the tray again. Finally, participants were advised to follow these instructions twice each day. The written instructions also stressed that participants should not use any other oral health products that contain a desensitizing agent.

DOI 10.1111/j.1708-8240.2011.00437.x © 2011 Wiley Periodicals, Inc.

Participants returned all used and unused syringes of the bleaching and desensitizing agents at each evaluation appointment during active bleaching. Participants' oral soft tissues were examined at each evaluation appointment and participants were asked about any possible complications. These procedures were completed to assure participants' safety.

Participants completed a daily diary for 1 week prior to bleaching, during 2 weeks of active bleaching and for 1 week after the end of bleaching. Anecdotally it has been reported that bleaching sensitivity ends almost immediately at the end of bleaching. Accordingly studies have not included bleaching sensitivity data beyond the active bleaching period. As an additional observation, the present study collected data on this issue. Similarly, many studies have not included measurement of a baseline or endemic level of tooth sensitivity that exists unrelated to bleaching. We have included this measurement for two reasons: First, to facilitate calculating a change in sensitivity from baseline levels—the study outcome. Second, the choice of this outcome simplifies the statistical testing.

The difference in tooth sensitivity levels from baseline to active bleaching was our outcome of interest. With this outcome each participant acts as his own control. Unlike the typical approach, these data set up one straight forward comparison of groups, rather than a comparison of groups and evaluations periods. Since there are simple, acceptable statistical procedures for testing the chosen outcome whether or not they are normally distributed, this approach avoids a multiple comparisons problem.

During active bleaching participants used the daily log to note the use of the whitening agent twice each day. Throughout the recording period, they noted the presence or absence of tooth sensitivity by checking the "Yes" or "No" box. Those who responded "yes" next recorded their overall assessment of tooth sensitivity that resulted from their normal daily activities. This was done using a VAS. Participants were instructed to mark the far right hand end of the line if the pain was "the worst you could imagine," or, if pain was less than that, to "place a mark anywhere along the line that represented what you felt." The scale consisted of a 100-mm line. The score was determined by measuring from the left hand edge of the line to the point where the participant's mark intersected the line. Scores were measured and recorded to the nearest millimeter. Completed logs were collected at each evaluation.

Color evaluations were performed to measure the degree of color change at baseline, immediately postbleaching and 6 weeks after the end of active bleaching. At each color evaluation an investigator and a trained research assistant each evaluated tooth color. Prior to the study research assistants and investigators underwent calibration exercises. The calibration exercise utilized two separate shade guides. Loose tabs from one guide were randomly arranged and their identifying label covered. The individual tabs were matched using the second, intact shade guide. Each evaluator was considered calibrated once he had attained 85% mastery on two separate tests.

Color change was assessed to investigate the possibility that use of the desensitizing agent might enhance or detract from the efficacy of the whitener. Color was evaluated using the Vita Classical and Vita Bleachedguide 3D shade guides (both Vident, Brea, CA, USA). The Bleachedguide 3D was included because compared with the Vita Classical it is more clearly ordinal in nature, and has more uniform color change from tab to tab. The tabs were numbered from darkest to lightest. The darkest tab was numbered 1 whereas the lightest tab was numbered 16 and 15, respectively, for the Classical and Bleachedguide. Tab change was calculated by subtracting the corresponding number for the tab chosen at baseline from that of the tab chosen at subsequent evaluations.

Study Outcomes

The daily log data was used to count the number of participants in each group that reported tooth sensitivity at any point during active bleaching. The outcome of interest was the proportion in each group.

For each group the daily logs were also used to count the number of days of sensitivity each participant

© 2011 Wiley Periodicals, Inc. *DOI 10.1111/j.1708-8240.2011.00437.x*

reported. Similarly, the number of days participants used the bleaching material was calculated. Finally, once the total of days of sensitivity and the total days of bleach use were determined, the proportion of day participants, as a group, experienced sensitivity was calculated.

For each participant the daily VAS scores were averaged. This was completed for all three data collection periods: the week preceding bleaching; the 2 weeks of active bleaching; and the week following the end of bleaching. Again, in terms of the VAS scores, the final outcome of interest was the change in average sensitivity score from baseline to active bleaching. For each participant the average score at baseline was subtracted from the average score during active bleaching. Thus a positive number represented an increase in sensitivity from baseline levels. A negative number indicated a decrease. As color rebound is common, the outcome of interest chosen is the color change from baseline to 6 weeks following the end of bleaching. Similar to the change in VAS score, the baseline tab number is subtracted from the tab number chosen at the final color evaluation.

Statistical Procedures

As the data were not normally distributed, the change in VAS score for the two groups was compared using a Mann–Whitney rank sum test. Comparisons of the percentage of participants experiencing sensitivity and the duration of sensitivity were compared using chi square tests. In order to maintain an overall significance level of 5%, individual significance levels for the three tests were set at 1.7%. All testing is identified within the text of the results and *p*-values reported.

RESULTS

For the whole 4-week period, the data regarding the percentages of participants experiencing tooth sensitivity at each evaluation are listed in Table 2. As this table considers each evaluation period individually some participants with sensitivity during multiple occasions are counted more than once. Regarding participants who reported sensitivity at some point during active bleaching, it was found that 51% of participants in Group zero-HAP and 29% of participants in Group n-HAP reported sensitivity. Here participants who experienced sensitivity at week one and week two are counted only once. Although the difference in percentage of participants experiencing sensitivity during the 2 weeks of active bleaching appears to be substantial, it was not statistically significant (chi square; $p = 0.06$).

TABLE 2. Number (percentage) of participants w sensitivity at each evaluation

Evaluation number	Group	Participants with sensitivity	Participants without sensitivity
Baseline	Zero-HAP	3 (14%)	18 (86%)
Week one bleaching	Zero-HAP	14 (67%)	7 (33%)
Week two bleaching	Zero-HAP	7 (35%)	13 (65%)
One week postbleaching	Zero-HAP	5 (25%)	15 (75%)
Baseline	n-HAP	2 (10%)	19 (90%)
Week one bleaching	n-HAP	8 (38%)	13 (62%)
Week two bleaching	n-HAP	4 (19%)	17 (81%)
One week postbleaching	n-HAP	4 (19%)	17 (81%)

n-HAP = nano-sized hydroxyapatite; zero-HAP = placebo.

There was no significant difference between groups during active bleaching (chi square; $p = 0.06$).

From the daily sensitivity logs, the number of days each group of participants experienced sensitivity was noted. Similarly, the number of days participants as a group bleached their teeth was recorded. Responses from participants who had not actively bleached on a particular day were not included in the analysis. Participants in Group n-HAP reported 36 days of sensitivity whereas those in Group zero-HAP reported 76. Significantly fewer days of sensitivity were reported by those in Group n-HAP (chi square; $p = 0.001$). The results for the whole 4-week reporting period are noted in Table 3.

The VAS data were used to gauge the intensity of pain encountered by participants as they went about their

DOI 10.1111/j.1708-8240.2011.00437.x
© 2011 Wiley Periodicals, Inc.

TABLE 3. Percentage of days associated with sensitivity

Evaluation number	Group	Days with sensitivity	Days without sensitivity
Baseline	Zero-HAP	9 (6%)	138 (94%)
Week one bleaching	Zero-HAP	50 (34%)	97 (66%)
Week two bleaching	Zero-HAP	26 (19%)	114 (81%)
One week postbleaching	Zero-HAP	16 (11%)	124 (89%)
Baseline	n-HAP	7 (5%)	140 (95%)
Week one bleaching	n-HAP	20 (14%)	127 (86%)
Week two bleaching	n-HAP	16 (11%)	131 (89%)
One week postbleaching	n-HAP	14 (10%)	133 (90%)

n-HAP = nano-sized hydroxyapatite; zero-HAP = placebo.

Participants in Group n-HAP experienced significantly more days of sensitivity during active bleaching (chi square; $p = 0.001$).

TABLE 4. Average daily visual analog scale scores for three periods measured

Group	Visit	Median	25%	75%
Zero-HAP	Week prior	0.00	0.00	0.00
n-HAP	Week prior	0.00	0.00	0.00
Zero-HAP	Active bleaching	2.14	0.00	3.00
n-HAP	Active bleaching	0.00	0.00	0.71
Zero-HAP	Postbleaching	0.00	0.00	0.11
n-HAP	Postbleaching	0.00	0.00	0.00

n-HAP = nano-sized hydroxyapatite; zero-HAP = placebo.

normal daily activities. The VAS data were not normally distributed. Table 4 lists the median VAS scores for the three periods measured: week prior to bleaching; period of active bleaching; and postbleaching. The change in VAS scores from baseline to active bleaching are reported in Table 5. Although the trend of these data indicate that Group n-HAP experienced lower VAS scores, there was no statistically significant difference between groups (Mann–Whitney rank sum test; $p = 0.16$). However, the statistical power for this comparison was below the accepted standard.

TABLE 5. Visual analog scale scores: average change from baseline

Group	Description	Median	25%	75%
Zero-HAP	Change at active bleaching	0.43	0.00	5.50
n-HAP	Change at active bleaching	0.00	0.00	0.89

n-HAP = nano-sized hydroxyapatite; zero-HAP = placebo.

TABLE 6. Mean tab number at each evaluation period

	Vita Classical Tab number	Bleachedguide Tab number
Zero-HAP		
Baseline	8.7	7.9
Immediate postbleaching	12.4	9.9
Six weeks postbleaching	13.1	10.0
n-HAP		
Baseline	9.0	7.4
Immediate postbleaching	12.5	9.8
Six weeks postbleaching	12.5	9.5

The two color change measures indicated positive whitening took place for both groups. The teeth were brighter immediate postbleaching and 6 weeks following the end of bleaching (Table 6). Using the Bleachedguide 3D, 6 weeks following the end of bleaching the mean tab changes from baseline were 2.2 and 2.0 for Groups zero-HAP and n-HAP, respectively. There was no significant difference between groups (*t*-test; $p = 0.85$). The Vita Classical shade guide results were similar. Mean tab changes were of 4.3 and 3.6 for Groups zero-HAP and n-HAP, respectively. There was no significant difference between the two groups 6 weeks following the end of bleaching (*t*-test; $p = 0.38$).

DISCUSSION

The three measures of tooth sensitivity chosen were intended to investigate three different and important aspects of sensitivity: the first is the likelihood that sensitivity will occur, the second is how long sensitivity

© 2011 Wiley Periodicals, Inc. *DOI 10.1111/j.1708-8240.2011.00437.x*

is likely to last, and the third is the intensity level that is likely to be incurred. In order to provide their patients with as much information as possible before obtaining their consent to treatment, practitioners need reasonable estimates of all three aspects.

In the present study, the placebo group, Group zero-HAP, is essentially a traditional whitener without any desensitizer. For whiteners without desensitizing ingredients in the formulation, reports of tooth sensitivity vary from 0 to 100%.[1,2] One study[3] reported 52%, whereas another[4] reported 13%. In a review of bleaching-related sensitivity articles Haywood's estimate was 67%.[17] Our finding that 51% of participants assigned to the placebo experienced tooth sensitivity is comparable with that reported in the literature.

The active treatment group, Group n-HAP, in this study is comparable with whitening agents containing a desensitizer. In a report of a whitener containing a desensitizing agent, the percentage of participants who reported tooth sensitivity was 23%.[6] Another study investigating two desensitizing formulations reported tooth sensitivity in 20 and 53% of subjects.[18] In a larger study[7] of whiteners claiming low sensitivity, 25% of participants reported tooth sensitivity. More specifically, 13% reported tooth sensitivity and 12% reported both gingival and tooth sensitivity.

The present result that 29% of participants in the group using the desensitizing agent experienced tooth sensitivity is consistent with the three studies cited earlier.[6,7,18] Given the differences in study designs, study populations, and research personnel, such comparison can only provide a limited reference point. Accordingly, the authors have not included product names from these other studies in order to avoid the appearance of making unwarranted comparisons.

The larger study cited earlier[7] investigated not only the percentage of participants who reported sensitivity but the duration of their sensitivity as well. The findings were that, out of 14 days total, 77% of participants experienced sensitivity on 3 or fewer days. More specifically, 53% did not experience sensitivity at any time and 22% reported sensitivity for 3 or fewer days.

As reports move beyond simple percentages of participants, one sees bleaching-related tooth sensitivity from a different perspective. Observing that 47% of participants experienced sensitivity one might conclude sensitivity is a more major issue. Observing that 77% of participants experienced no sensitivity at all or sensitivity of only 3 or fewer days, one might conclude sensitivity was a more minor issue. When one considers both figures the perception changes. While the majority experiences little bleaching sensitivity, for a minority of participants the experience is far different. Further, it is clear that this wide variation in experience from participant to participant makes it difficult to study this issue.[7]

Several studies have included measurement of the duration of sensitivity.[5–7] A small clinical trial of three low-sensitivity whiteners found that two were not associated with any tooth sensitivity. Participants using the third agent experienced tooth sensitivity on 14% of the total days spent bleaching.[5] The other studies reported tooth sensitivity over 12%[6] and 14% of the total days spent bleaching.[7] In the present study, the group using the desensitizer reported only 14%. This was consistent with the other studies of low-sensitivity whiteners cited. By contrast, the participants in the placebo group reported tooth sensitivity over 36% of the total days spent bleaching.

In terms of the duration of sensitivity there was a statistically significant difference between groups. Despite what appears to be important clinical differences between the groups for the other two measures of sensitivity reported, the differences were not statistically significant. Although data from a previous study were used to calculate the sample size required, the mean responses for the present study were much lower and the variation from participant to participant was larger than expected. Accordingly, for the other two comparisons the study lacked sufficient statistical power.

The lack of statistical power makes interpreting the results of the present study difficult. Where statistical power is sufficient, the results of hypothesis testing from a double-blind, randomized clinical trial can be

 DOI 10.1111/j.1708-8240.2011.00437.x © 2011 Wiley Periodicals, Inc.

relied upon as relevant, high-quality evidence that practitioners can confidently incorporate into their treatment regimens. The lack of statistical power makes both of two possible interpretations reasonable. First, based on the statistical testing, the desensitizer offered no clinical benefit in lessening the incidence and intensity of bleaching-related tooth sensitivity. Second, based on the data trend, although the study was unable to demonstrate it, there was a clinically important benefit.

The authors believe taking an evidence-based treatment approach will be beneficial. It is a tenet of evidence-based dentistry (or best-evidence treatment) that practitioners do not have the luxury of waiting for perfect data. Rather their obligation to serve their patients means that, from among whatever levels of evidence are available they must choose the best and act, thus the term best-evidence. The hypothesis that the duration of tooth sensitivity would be lower in the n-HAP group was confirmed statistically. From an evidence-based treatment perspective this is Ib or the second highest level of evidence. The previously available evidence regarding the efficacy of an n-HAP paste was from laboratory studies and anecdotal reports. This is level IV or the lowest level of evidence. The present study provides level III evidence that the n-HAP paste was effective at lowering the incidence and intensity of tooth sensitivity.

Another tenet of best-evidence treatment is that one must be open to discarding lower level evidence once higher level evidence becomes available. That is good advice in this case as well.

For the other two measures practitioners should consider the clinical question unsolved, use their best judgment given the available evidence, and be open to a reassessment as new data becomes available.

CONCLUSION

Within the limits of the study it can be concluded that use of a nano-hydroxyapatite paste following application of a tooth whitening agent was associated with a statistically significant reduction in the duration of tooth sensitivity.

DISCLOSURE AND ACKNOWLEDGEMENTS

None of the authors has a financial interest in any of the companies or products used in this article. This project was supported by a grant from Sangi Co., Ltd., Tokyo, Japan.

REFERENCES

1. Reinhardt JW, Elvins SE, Swift EJ, Denehy GE. A clinical study of nightguard vital bleaching. Quintessence Int 1993;24:379–84.
2. Sterret J, Price RB, Bankey T. Effects of home bleaching on the tissues of the oral cavity. J Can Dent Assoc 1995;61:412–20.
3. Haywood VB, Leonard RH, Nelson CE, Brunson WD. Effectiveness, side effects and long-term status of nightguard vital bleaching. J Am Dent Assoc 1994;125:1219–26.
4. Leonard RH, Haywood VB, Phillips C. Risk factors for developing tooth sensitivity and gingival irritation associated with nightguard vital bleaching. Quintessence Int 1997;28:527–34.
5. Pohjola RM, Browning WD, Hackman ST, et al. Sensitivity and tooth whitening agents. J Esthet Restor Dent 2002;14:85–91.
6. Browning WD, Chan DCN, Frazier KB, et al. Safety and efficacy of a nightguard bleaching agent containing sodium fluoride and potassium nitrate. Quintessence Int 2004;35:693–98.
7. Browning WD, Blalock JS, Frazier KB, et al. Duration and timing of sensitivity related to bleaching. J Esthet Restor Dent 2007;19:256–64.
8. Kihn PW, Barnes DM, Romberg E. A clinical evaluation of 10 percent carbamide peroxide tooth-whitening agents. J Am Dent Assoc 2000;131:1478–84.
9. Matis BA, Mousa HN, Cochran MA, Eckert GJ. Clinical evaluation of bleaching agents of different concentrations. Quintessence Int 2000;31:303–10.
10. Matis BA, Wang Y, Jiang T, Eckert GJ. Extended at-home bleaching of tetracycline-stained teeth with different concentrations of carbamide peroxide. Quintessence Int 2002;33:645–55.
11. Browning WD, Chan DC, Myers ML, et al. Comparison of traditional and low sensitivity whiteners. Oper Dent 2008;33(4):379–85.

© 2011 Wiley Periodicals, Inc. *DOI 10.1111/j.1708-8240.2011.00437.x*

12. Giniger M, MacDonald J, Ziemba S, Felix H. The clinical performance of professionally dispensed bleaching gel with added amorphous calcium phosphate. J Am Dent Assoc 2005;136(3):383–92.
13. Kawamata H, Fujita K, Ishizaki T, et al. A new enamel restoring agent for use after bleaching. J Dent Res 2004;83(Special Issue B):Abstract #1919.
14. Takikawa R, Fujita K, Ishizaki T, Hayman R. Restoration of post-bleach enamel gloss using a non-abrasive, nano-hydroxyapatite conditioner. J Dent Res 2004;85(Special Issue B):Abstract #1670.
15. Toko T, Tamaoka K, Imaizumi A, et al. After-bleach treatments for reducing roughness by SPM. J Dent Res 2004;85(Special Issue B):Abstract #1686.
16. Yarborough DK. The safety and efficacy of tooth bleaching: a review of the literature 1988–1990. Compend Contin Educ Dent 1991;12(3):191–6.
17. Haywood VB. Current status of night-guard vital bleaching. Compendium 2002;21(Suppl 28):S10–7.
18. Nathoo S, Santana E, Zhang YP. Comparative seven-day clinical evaluation of two tooth whitening products. Compend Contin Educ Dent 2001;22:599–606.

Reprint requests: William D. Browning, DDS, MS, DS S-317, 1121 West Michigan Street, Indianapolis, IN 46202, USA; Tel.: 317-274-3640; Fax: 317-278-2818; email: wbrownin@iupui.edu

This article is accompanied by commentary, Effect of a Nano-Hydroxyapatite Paste on Bleaching-Related Tooth Sensitivity, Laura Tam, DDS, MSC

DOI 10.1111/j.1708-8240.2011.00438.x

 DOI 10.1111/j.1708-8240.2011.00437.x © 2011 Wiley Periodicals, Inc.

Copyright of Journal of Esthetic & Restorative Dentistry is the property of Wiley-Blackwell and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.