Remineralization Potential of a Fluoridated Carbamide Peroxide Whitening Gel

JASON GLADWELL, DDS*
DARRIN SIMMONS†
J. TIMOTHY WRIGHT, DDS, MS‡

ABSTRACT

Purpose: Little knowledge exists regarding the potential remineralizing benefits of adding fluoride to carbamide peroxide-based whitening gels. The aim of this project was to evaluate whether a whitening system with fluoride will remineralize previously demineralized enamel.

Materials and Methods: Twenty-four extracted teeth were sectioned into quadrants labeled A to D. Tooth quadrants in groups A, B, and D were demineralized with a lactic acid, methyl-cellulose gel system to mimic incipient carious lesions. Group C was neither demineralized nor treated. Group D was demineralized, but not treated with a whitening gel. Groups A and B were exposed to one of two commercially prepared 10% carbamide peroxide whitening gels: one that was fluoride free (group A) and one that contained fluoride (0.463%NaF) (group B). Remineralization was evaluated histologically and analyzed statistically using paired *t* tests accepting $p < 0.05$ as significant.

Results: Shade comparisons showed equal whitening efficacy of both gel A and B. Paired *t* tests show a significant reduction in lesion depth after treatment with the fluoride containing gel (B: mean lesion depth = 100 μm; $p < 0.01$), while there was no difference for the gel lacking fluoride (A: mean lesion depth = 110 μm).

Conclusion: Under the conditions of this study, the addition of fluoride to a tooth whitening system does not affect the gel's whitening efficacy. The addition of fluoride could provide remineralization properties to the gel. As tooth whitening therapies continue to grow and evolve, a strong focus should rest on improving these materials in ways that will provide ever greater patient benefits. Coupling the esthetic benefits of whitening with the preventive benefits of fluoride is a natural step in this direction.

CLINICAL SIGNIFICANCE

Therapuetic quantities of fluoride can impact remineralization properties of commercially available tooth whitening gels without altering whitening properties.

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INTRODUCTION

As seen through the recent introductions of products such as Crest White Strips (Procter & Gamble, Cincinnati, OH, USA) and Colgate Simply White (Colgate, Piscataway, NJ, USA), patients are increasingly interested in enhancing the esthetics of their smiles. The popularity of dentifrices marketed to decrease dental caries also indicates that consumers of dental

*Dental Research Center; Pediatric Dentistry, University of North Carolina, School of Dentistry, Chapel Hill, NC, USA
†Dental Research Center; Pediatric Dentistry, University of North Carolina, School of Dentistry, Chapel Hill, NC, USA
‡Dental Research Center; Pediatric Dentistry, University of North Carolina, School of Dentistry, Chapel Hill, NC, USA

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products are concerned with keeping their mouth free of decay. From these observations one can presume that patients would regard a whitening system that also fights decay as being of higher value than one that only whitens teeth. Based on consumer trends of esthetic and therapeutic dental products over the past decade, it is highly likely that commercial demand would exist for a material that would have both a bleaching and caries reduction benefit.

There are currently numerous different whitening systems available, ranging from those based on carbamide peroxide to those with hydrogen peroxide.[1] While the product names and marketing are slightly different, the underlying mechanism of action is essentially the same: the lightening of a tooth through the application of a chemical agent to oxidize the organic pigmentation in the tooth.[2]

Fortunately, extensive research related to systems directed at nonvital bleaching, vital bleaching, nightguard bleaching, and dentifrice-based whitening have been completed helping validate the effectiveness and safety of these approaches. Based on these previous works, it is evident that the whitening effect of bleaching solutions is time and concentration dependent.[3]

One problem with today's whitening systems is that as efforts have been made to increase patient benefits in terms of better whitening efficacy and ease of use, little has been done with regard to strengthening the teeth that are being whitened. Fluoride already has been proven to be useful when added to other commonly used dental products such as dentifrices and mouth rinses.[4] These applications show the added patient benefits of low-dose high-frequency fluoride, and lend credibility to the argument of adding fluoride to whitening systems to aid in remineralization.[5,6] The addition of fluoride has also been shown to decrease tooth sensitivity often associated with whitening, while not significantly changing the efficacy of the gel used.[7]

This area of research is potentially very important and could have significant clinical implications. If remineralization is possible through the use of a whitening system, these systems could serve the dual role of improving esthetics while also acting as a caries-preventive measure. Increasing the benefits from whitening alone to whitening with the possibility of decreasing a patient's caries risk, as well as further limiting sensitivity experienced during treatment, are steps in the right direction, but should by no means be considered an end point. The present study was aimed at determining whether the addition of fluoride to a whitening gel could promote remineralization of simulated enamel demineralization.

MATERIALS AND METHODS

Extracted teeth were collected over a period of a month through the cooperation of local oral and maxillofacial surgeons and the University of North Carolina (UNC) Oral and Maxillofacial Surgery Department. The extracted third molars used in this study were limited to those without previous restorations or fractures. Exclusion criteria also include teeth with fluorosis, enamel, or dentin defects. All teeth were scaled to remove tissue and other debris and kept hydrated in a phosphate buffered saline solution (PBS) until they were prepared for testing. Twenty-four third molar teeth were used in the project. The pretreatment shade was determined using a Vita Classical shade guide (Vita Zāhnfabrik, Bad Sackingen, Germany). The pretreatment shades were established by one observer using natural light to avoid metamerism.[8] In instances when a tooth was between shades, the lighter of the two shades was recorded.

After the initial shades were determined and recorded, the roots were amputated and the crowns of the teeth were sectioned into quadrants. The teeth were sectioned using a slow speed dental handpiece and diamond sectioning disk. The crowns were sectioned mesiodistally

and faciolingually in a manner that would allow each quarter to be approximately the same size as the others. Once sectioned, one quarter was randomly assigned and designated as belonging to either group A, B, C, or D. This experimental approach allowed each tooth to serve as its own control thereby helping reduce the effects of uncontrollable confounders related to inherent differences in the structure and composition of individual teeth.

Figure 1 shows a flow chart of the sequence of treatment for each tooth used in the study. Groups A and B were treated with the demineralizing solution followed by treatment with whitening gel (one gel with fluoride and the other without fluoride). Group C was the untreated, nondemineralized experimental control. Because no further treatment other than sectioning would be necessary for group C, these sections remained hydrated in individual containers with 2 mL PBS solution until the other groups were ready for histologic evaluation. Group D was treated with the demineralizing solution, but were not treated with either whitening gel. Groups A, B, and D were then exposed for 1 week to a 10% (w/v) methylcellulose gel acidified with 0.1 *m* lactic acid-sodium lactate at pH 4.5 and having a hydroxyapatite content of 0.05% (w/v). The sections were placed in individual glass containers with 2 mL of the demineralizing solution. This same demineralizing solution was used in past research by Kotsanos, Levers, and Tyler, simulating natural enamel caries in vitro, which are indistinguishable from natural enamel caries when examined by polarized light microscopy and contact microradiography.[9]

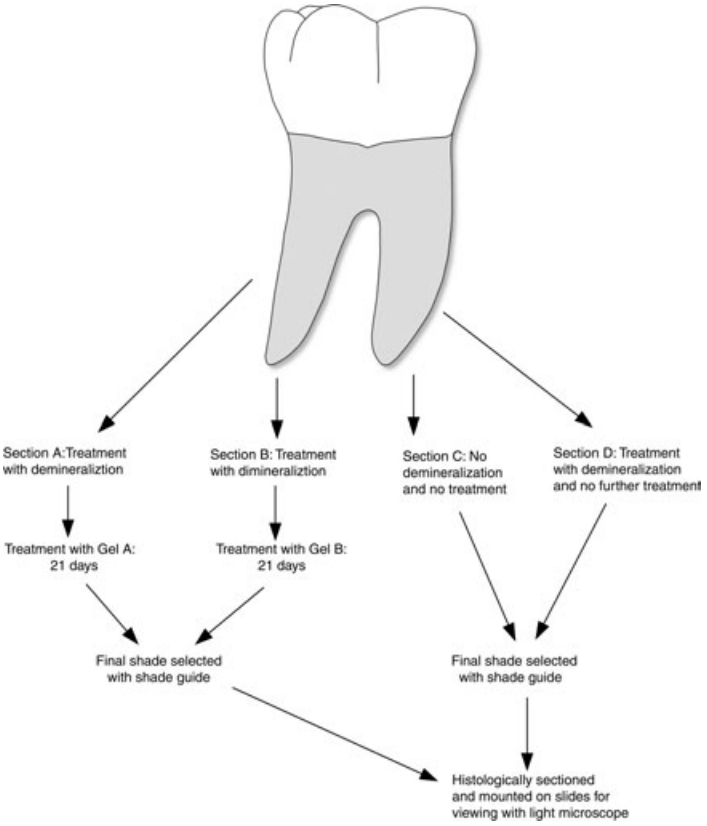

Figure 1. Flow chart illustrating the experimental design evaluating the difference in remineralization potential of whitening gels with and without fluoride.

After 1 week, the tooth quadrants from groups A, B, and D were removed from the demineralizing solution, rinsed with deionized water, and cleaned with a soft-bristled toothbrush to remove any residual gel. The tooth quadrants were then returned to individual labeled containers containing 2 mL PBS solution. Because no further treatment other than sectioning would be necessary for group D, these sections remained hydrated in individual containers with 2 mL PBS solution until the other groups (A and B) had been treated with the whitening gel and were ready to be sectioned for histologic evaluation.

Tooth quadrants in groups A and B were treated for 8 hours per day for

21 days with their corresponding whitening gel. The whitening gels were both 10% carbamide peroxide-based gels (Opalescence, Ultradent Products, Inc., South Jordan, UT, USA). The gels were not identified as to fluoride content so the investigator was masked as to the control and experimental gel until after scoring of all samples. The whitening gels were purchased by Procter & Gamble and modified by the addition of fluoride to one of the gels. Once fluoride was added to one of the gels, both groups of whitening gels were repackaged and labeled to maintain the blindness of the study. The concentration of fluoride in the study was used because of its close correlation to prescription strength products already used in caries prevention today. Tooth samples in groups A and B were brushed with a soft-bristled toothbrush and deionized water after each 8-hour whitening treatment to remove residual gel and placed into the PBS solution for 16 hours and the whitening gel treatment then repeated for 21 days.

Final shade determination was made after the 21 treatments on all tooth quadrants using the same Vita shade guide with natural light (Figures 2 and 3). After all treatments and posttreatment shade determination, all tooth quadrant samples were sectioned with a slow-speed sectioning saw with deionized water coolant, polished to appropriate thickness (approximately 150 µm), and mounted on histologic slides for evaluation of lesion depth with light microscopy.

Zones of enamel demineralization were measured using a computer imaging program. The width of the zone of demineralization was measured at five different points, all equidistant, and then averaged to determine the mean lesion depth for each sample (Figure 4). Differences in lesion depths between the groups were evaluated using *t* tests accepting ≤0.05 as significant. After evaluation of shade changes and lesion depths, the fluoride content of the whitening gels was determined.

RESULTS

Fluoride analysis revealed that gel A had no fluoride and gel B was fluoridated. Differences in lesion depths were significantly reduced ($p = 0.002$) in group B (Opalescence, 10% carbamide peroxide with

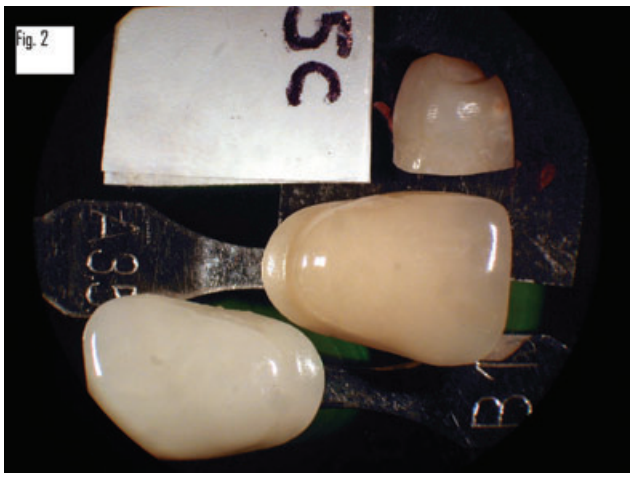

Figure 2. Initial shade of a control sample in group C shown next to the corresponding Vitapan shade tab. The final shade of this same tooth from group A (no fluoride) shows a reduction in color from shade A3.5 to shade B1, which was the average shade change in both bleaching groups.

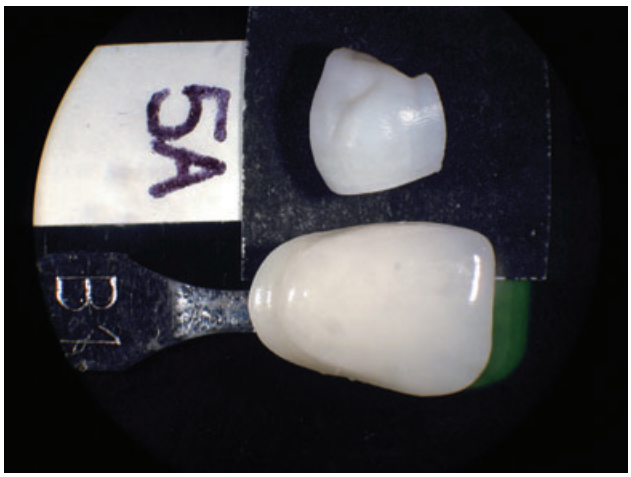

Figure 3. Section A of sample #5, postwhitening treatment. This shows the sample whitening to shade B1 on the Vitapan shade guide.

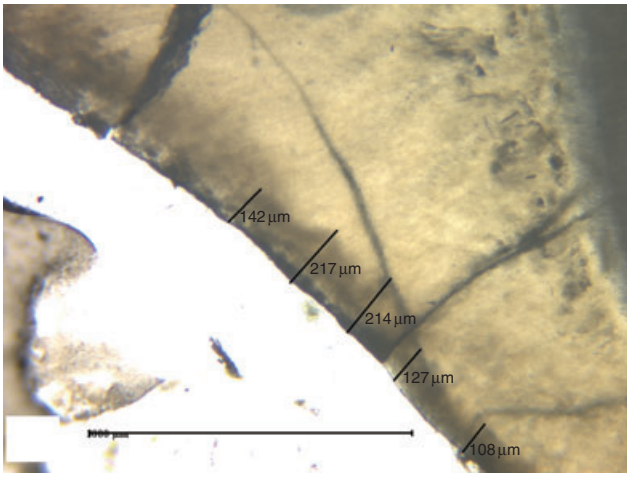

Figure 4. Light micrograph of a thin section illustrating the five measurements taken per sample section and the calibrated ruler used for determining the lesion depth.

TABLE 1. SUMMARY OF SIGNIFICANT RESULTS

Experimental Results	Sample	Group A	Group B	Group D
Mean lesion depth (µm) (±SD)	24	109 ± 37.5	99 ± 43.3	127 ± 43.4
Fluoride treatment		No	Yes	No
p value		0.07	0.002	

These results show the changes in mean lesion depth of samples treated with the fluoridated gel B were statistically significant compared with the control group D. It also shows the samples treated with the nonfluoridated gel A lacked statistical significance with respect to decrease in mean lesion depth.

0.463% NaF) compared with demineralization only (group D). As shown in Table 1, the mean lesion depth was less in group A compared with the demineralized, no-bleach control group D; however, the difference was not statistically significant. The whitening efficacy was not altered by the addition of fluoride to gel B. The teeth had a variety of pretreatment shades ranging from A3 to C4. Both gels whitened teeth with an average starting shade of A3.5 to a final shade of B1. The sample size in this study included 24 extracted third molars and used highly sensitive parametric measurements (continuous measurement of lesion depth), providing sufficient power to identify significant differences of 15% lesion depth at the 95% confidence level.

DISCUSSION

This study reveals that the addition of fluoride to a 10% carbamide peroxide whitening gel does impart some potential for remineralization of demineralized enamel. Although this study did not attempt to pinpoint the exact mechanism of how the fluoridated whitening gel would remineralize tooth structure, it is believed by the authors that fluoride efficacy might well be potentiated by the bleaching components. Once the proteins that adhere to the enamel crystallites are removed by the bleaching agent, the reactive fluoride ion could interact with the freshly cleaned crystallites, thereby enhancing the potential for remineralization. This mechanism could be of benefit in cases where the lack of mineral results from demineralization as in the case of dental caries or a developmental defect that results in enamel hypomineralization and protein retention. It is also possible that the addition of fluoride to a whitening gel that enhances mineral deposition could help reduce the tendency for teeth to re-stain and darken over time. Increased mineral deposition would reduce the intercrystallite spaces in enamel, thereby reducing the potential for the reintroduction of proteins that change the enamel optical properties.

This study did not identify the threshold dose of fluoride needed to produce these results. In this study, 0.463% NaF was added to Opalescence 10% carbamide peroxide

whitening gel and no other concentrations of fluoride were examined. This study also examined only third molars and could yield different results if anterior teeth were used. Future research should focus on determining the optimal concentration of fluoride that would render the desired best clinical results. Future research may also expand upon the many previous works that examine surface changes and microhardness of teeth as related to different whitening products with and without the addition of fluoride in higher concentration than currently used. PBS solution was used as the method of keeping each sample hydrated throughout the length of the study. Perhaps, either natural saliva or a natural saliva substitute should be used as the hydrating medium to provide the minerals and environment that may better replicate the environment of the oral cavity. Although all groups were exposed to the same environment (except for groups A and B, which were treated with the whitening gels), the experiment did not examine the possibility of remineralization from regular oral hygiene practices and the natural environment of the oral cavity. Clearly, clinical trials to evaluate the effect of fluoridated whitening gels are necessary to confirm whether there is a potential benefit in caries protection or increased stability of the bleaching effect.

CONCLUSIONS

Under the conditions of this study, the whitening efficacy was not altered by the addition of fluoride to the whitening gel. Simulated areas of demineralization did, however, show statistically significant levels of remineralization when treated with the whitening gel containing fluoride versus the gel without fluoride.

CLINICAL IMPLICATIONS AND RELEVANCE

In an ever increasing esthetically oriented society, it is the obligation of the dental care provider to ensure that all necessary precautions are being taken to provide maximum benefit and safety to the patient. This obligation extends to areas of elective care including tooth whitening. As tooth whitening therapies continue to grow in popularity and evolve in therapeutic application, the focus should rest on improving the materials in ways that will provide ever greater patient benefits by incorporating fluoride into whitening products. However, the proven benefits of fluoride are still protested against and debated by a small segment of the population; the addition of fluoride to a whitening gel would probably not be a welcomed benefit for them. As with any fluoride-containing product, care should always be taken to ensure that high fluoride levels are not experienced during critical tooth developmental periods, in which the adverse effects of fluorosis may be experienced. The high concentration of fluoride added to the whitening gel used in the study could potentially be enough to cause fluorosis of the dentition if used for a long enough period of time during tooth development. Benefits could include a reduction in the potential caries risk, remineralization of incipient carious lesions, reduction in enamel solubility by increasing the fluoride content of the carbonate-substituted hydroxyapatite enamel cystallites, or decreasing sensitivity. Coupling the esthetic benefits of whitening with the preventative benefits of fluoride is a natural step in this direction.

DISCLOSURE

This study was funded in part by the UNC School of Dentistry, the AADR/IADR Student Research Fellowships, and Procter & Gamble.

REFERENCES

1. Gerlach RW, Gibb RD, Sagel PA. A randomized clinical trial comparing a novel 5.3% hydrogen peroxide whitening strip to 10%, 15%, and 20% carbamide peroxide tray-based bleaching systems. Compend Contin Educ Dent Suppl 2000 Jun;29:S22–8.

2. Roberson T, Heymann H, Swift E Jr. Sturdevant's art and science of operative dentistry. 4th ed. St. Louis (MO): CV Mosby, Inc. 2002.

3. Heymann HO. Tooth whitening: facts and fallacies. Br Dent J 2005;198:514.

4. Zimmer S, Jahn KR, Barthel CR. Recommendations for the use of fluoride in

caries prevention. Oral Health Prev Dent 2003;1(1):45–51.

5. Negri HM, Cury JA. Dose-response effect of a dentifrice formulation with low fluoride concentration—an in vitro study. Pesqui Odontol Bras. 2002;16(4):361–5.

6. Twetman S, Axelsson S, Dahlgren H, et al. Caries-preventive effect of fluoride toothpaste: a systematic review. Acta Odontol Scand 2003;61(6):347–55.

7. Tam L. Effect of potassium nitrate and fluoride on carbamide peroxide bleaching. Quintessence Int 2001;32(1):766–70.

8. Grajower R, Revah A, Sorin S. Reflectance spectra of natural and acrylic resin teeth. J Prosthet Dent 1976;36(5):570–9.

9. Kotsanos N, Durling A, Leuers B, Tyler S. Simulation of natural enamel caries in vitro with methylcellulose acid gels: effect of addition of calcium and phosphate ions. J Biol Buccale 1989;17(3):159–65.

Reprint requests: Dr. J. Timothy Wright, DDS, MS, 301 Dental Research Center, School of Dentistry, UNC Chapel Hill, Pediatric Dentistry CB #7450, Chapel Hill, NC 27599–7450; Tel.: (919) 966–8822; email: Tim_wright@dentistry.unc.edu

COMMENTARY

REMINERALIZATION POTENTIAL OF A FLUORIDATED CARBAMIDE PEROXIDE WHITENING GEL

Van B. Haywood, DMD*

The authors have presented some interesting data concerning the potential for fluoride remineralization of demineralized enamel while effectively bleaching the tooth. Most interesting is the proposal that bleaching could improve the efficacy of the fluoride due to the cleaning nature of bleaching. They have correctly cited the limitations of this study in that it is on extracted teeth and the teeth were not stored in artificial saliva. The lack of normal biological mediums may have exaggerated the potential benefit of the fluoride-containing product, as some benefits of remineralization would have occurred from saliva in the nonfluoride group.[1] However, there are other articles citing the beneficial effects of fluoride in bleaching solutions for which this article is an additional confirmation.[2–6]

It is unfortunate that the authors did not treat all the samples the same. According to figure 1, a group C was also evaluated, yet table 1 gives no data as to the amount of or lack of demineralization. The text states that all groups were evaluated, but the table does not indicate the outcome. The reason for this concern is that if the teeth were already demineralized to some degree, then the effect of the solution would be the amount of acid demineralization (D) minus the amount of existing demineralization (C), not D alone. We do not know if this would change the significance of the data. Also, the authors did not brush D after demineralization of the tooth, but did brush both bleaching groups A and B. The concern here is that the lack of lesion depth on the bleached samples could be a result of the brushing away of the softened demineralized surface of A and B. We know nothing of the amount and time of brushing, the hardness of the brush, and the force of application. Without the positive control C, and with the nonbrushing of D, we do not know if the reduced surface depth was due to the action of fluoride or the loss of depth from brushing.

The authors cite a statistical difference between the untreated demineralized group D and the fluoride-containing bleaching group B. However, we are not told whether there is any significant difference between bleaching product A without fluoride and bleaching product B with fluoride measurements. We can see that there is a numerical difference, but we do not know if this is statistically or clinically different. The authors also state the sample sites for measuring depths were equidistant apart, but the figure shown does not demonstrate that claim. It is unknown how the starting point of the measurement was obtained, and what determined what sites were measured. When the difference in treated and control are only 25 microns, small variances in technique could radically alter the outcome.

The authors point out there is no difference in bleaching efficacy, which is an additional insight to the original article by Tam and colleagues in *Quintessence International* in 1991 refuting the earlier concern that fluoride would hinder the efficacy of the bleaching treatment. Her article was a clinical study. In this laboratory study, the shade was taken prior to sectioning the teeth, which may alter the baseline. Apparently, group C was used as the color standard to demonstrate bleaching, although that is not cited in the text. It was good that each tooth served as its own control, as the response of individual teeth varies greatly.

What is most interesting is to note the variations in amount of demineralization on a single tooth surface when exposed to the most ideal condition. This insight helps explain to the dentist the somewhat random nature of demineralization clinically, where the entire tooth is not being brushed but only one spot has caries. In some areas, the demineralization was twice as deep as on other areas.

We are not given a rationale for the 0.463% NaF that was added other than it is the amount typically used for caries prevention. There is no reference to that statement, and this formulation used in this study may not be commercially available to the clinician, as the amount was added to Opalescence (Ultradent Products, Inc., South Jordan, UT). The amount of fluoride in Opalescence PF bleaching material (Ultradent Products, Inc.) is 0.25% NaF, the amount in Flor-Opal Fluoride varnish (Ultradent Products, Inc.) is 5.0% NaF, and the amount in PreviDent 5000 (Colgate Oral Pharmaceuticals, Piscataway, NJ, USA) is 1.1% NaF. Gel-Kam Gel (Colgate Oral Pharmaceuticals) has 0.4% SnF_2. We do not know how this percentage of fluoride compares to the ppm data for water and other materials, and what is the expected remineralization from a topical application of fluoride done after the bleaching treatment. Another possible use for group C would have been to demineralize it as well, and then treat it with conventional fluoride after each bleaching application to see if that was more effective than fluoride in the bleaching material.

The authors have pointed out the concern for too much fluoride by some people. It would seem the addition of fluoride for the sake of remineralization would be applied in patients who have demineralized teeth, such as in poor oral hygiene and postorthodontic patients. There is also data showing some reduction in enamel hardness from some bleaching, for which the use of fluoride is most appropriate in bleaching. In summary, based on this work and the other articles cited, the addition of fluoride seems to be a beneficial component of a bleaching material.

REFERENCES

1. Justino LM, Tames DR, Demarco FF. In situ and in vitro effect of bleaching with carbamide peroxide on human enamel. Oper Dent 2004;29(2):219–25.
2. Basting RT, Rodregues AL Jr., Serra MC. The effect of 10% carbamide peroxide bleaching material on microhardness of sound and demineralized enamel and dentin in situ. Oper Dent 2001;26:531–9.
3. Lewinstein I, Fuhrer N, Churaru N, Cardash H. Effect of different peroxide bleaching regimens and subsequent fluoridation on the hardness of human enamel and dentin. J Prosthet Dent 2004;92:337–42.
4. Clark LM, Barghi N, Summitt JM, Amaechi BT. Enamel fluoride uptake from fluoridated carbamide peroxide bleaching gel. AADR Abstract #0498 2006.
5. Al-Qunaian T. The effect of whitening agents on caries susceptibility on human enamel. Oper Dent 2005;30(2):265–70.
6. Clark LM, Barghi N, Summitt JB, Amaechi BT. Influence of fluoridated carbamide peroxide bleaching gel on enamel demineralization. IADR Abstract #0497 2006.

**Professor, director of Dental Continuing Education, Department of Oral Rehabilitation, School of Dentistry, Medical College of Georgia, Augusta, GA, USA*