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ABSTRACT

Background. The authors conducted a study to evaluate tooth sensitivity (TS) and the bleaching effectiveness associated with use of a calcium-containing (CC) in-office bleaching gel.

Methods. The authors used a 35 percent calcium-free (CF) hydrogen peroxide gel and a 35 percent CC hydrogen peroxide gel according to the manufacturer's instructions in 40 caries-free participants 18 years or older. They performed two bleaching sessions with a one-week interval between sessions. The authors registered the color at baseline and after the first and second bleaching sessions by using a shade guide and by gauging the participant's perception of TS as registered on a scale from 0 (none) to 4 (severe). The authors evaluated the bleaching effectiveness at each week's recall visit by means of the Friedman test, and they compared the groups at each assessment point by means of the Mann-Whitney test. They evaluated the percentage of participants with TS and the intensity of the TS by using the Fisher exact and Mann-Whitney tests.

Results. Both groups demonstrated equivalent and significant tooth color enhancement compared with color values at baseline ($P < .05$), with an average bleaching of 7 to 8 shade guide units. Most of the participants from the CF group (80 percent) experienced sensitivity while undergoing the bleaching regimen,whereas only 40 percent of participants from the CC group reported experiencing TS ($P = .02$). The intensity of TS was significantly higher ($P < .01$) for the CF group during in-office dental bleaching.

Conclusions. The CC 35 percent hydrogen peroxide gel reduced the TS during in-office dental bleaching without jeopardizing the bleaching effectiveness.

Clinical Implications. The results of this study support the findings that a CC 35 percent hydrogen peroxide gel can reduce TS during in-office dental bleaching.

Key Words. Clinical protocols; dentin sensitivity; tooth bleaching.

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Although vital bleaching with a peroxide gel generally is recognized as both safe and effective, transient dentinal hypersensitivity is a common, unpleasant adverse effect of the treatment.[1] Patients undergoing bleaching procedures frequently complain of painful or uncomfortable sensations in the treated teeth,[2-4] probably caused by temperature change. Tooth sensitivity (TS) arising from vital tooth bleaching may be the result of the insult of hydrogen peroxide to the pulpal tissue after a 45-minute exposure[5]; it also may result from the direct activation of neuronal receptors,[6] such as the neuropeptide substance P, which is involved in the vasodilation and increased pulpal blood flow that allows the rapid release of a large number of inflammatory cells and mediators into the site of inflammation.[7]

Investigators have demonstrated that the preliminary use of desensitizing agents such as fluorides and potassium nitrate before at-home[8,9] and in-office[3] bleaching can reduce the experience of TS during the bleaching treatment. However, this approach adds another step to the bleaching protocol.

Manufacturers have attempted to reduce bleaching-related TS without

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adding an extra step to the protocol by adding desensitizing agents (such as fluorides and potassium nitrate) to the formulation of bleaching gels.[10-12] However, the benefits of this inclusion remain somewhat unclear, because investigators in studies of these agents reached conflicting conclusions.[10-12]

Because of such results, investigators started using other approaches to reducing TS that results from bleaching. Amorphous calcium phosphate was developed to remineralize teeth and reverse early enamel caries lesions, and Yengopal and Mickenautsch[13] confirmed its short-term effect in a 2009 meta-analysis. This positive effect on enamel remineralization has led some manufacturers to add this compound to at-home bleaching gels. Few clinical study investigators have addressed the benefits of this compound for reduction of TS in at-home bleaching,[10,14] and although investigators in one study demonstrated some statistical benefit,[14] the reduction in TS may not be clinically relevant and has received criticism.[15]

Investigators in some in vitro studies demonstrated the effects of including other types of calcium-containing (CC) compounds in bleaching gels with the aim of preventing the mineral loss and reduction in enamel microhardness produced by bleaching.[16-18] If these CC components prevent mineral loss, one may speculate that hydrogen peroxide penetration may occur at a lower diffusion rate, thereby reducing the absolute risk or intensity of TS. To our knowledge, no clinical study investigators have evaluated the clinical benefits of such inclusion. Therefore, we conducted a randomized clinical trial to assess the whitening efficacy and the self-assessed TS associated with use of a commercially available 35 percent hydrogen peroxide gel containing 2 percent calcium gluconate compared with those associated with use of a calcium-free (CF) 35 percent hydrogen peroxide gel.

METHODS

The scientific review committee for human participants at the School of Dentistry, University Estadual de Ponta Grossa, Ponta Grossa, Paraná, Brazil, approved this double-masked, parallel-group randomized clinical trial. Both the participant and the examiner who assessed the color change were masked as to the procedure—that is, neither of them knew which bleaching gel had been used. On the basis of preestablished criteria, we recruited participants by posting fliers in the university and sending e-mails. We selected 40 students from the same university. The study took place in the dental school's clinic from March 2009 through April 2010. Two weeks before the bleaching procedures, each participant signed an informed consent form and received a dental screening and a dental prophylaxis with pumice and water in a rubber cup.

Inclusion and exclusion criteria. Participants included in this clinical trial were at least 18 years old and had good general and oral health. We required that participants have six caries-free maxillary anterior teeth without facial restorations and that their upper maxillary incisors be of shade C2 or darker as judged by two clinicians (S.K. and A.R.) by means of comparison with a value-oriented shade guide (Vita Classical, Vita Zahnfabrik, Bad Säckingen, Germany). We excluded from the study potential participants who had undergone tooth-whitening procedures, had facial restorations, were pregnant or lactating, had severe internal tooth discoloration (as a result of tetracycline stains, fluorosis or pulpless teeth), or had bruxism habits or any other condition that could cause sensitivity (such as recession or dentin exposure), because they would not be eligible for a cosmetic treatment such as bleaching. We used the criteria described in a TS evaluation form, which we administered the week before beginning the bleaching therapy, to ask the participants about any previous sensitivity. We also excluded potential participants with TS considered mild or more severe.

Sample size calculation. Some investigators reported the absolute risk of TS to be approximately 86 percent for the CF bleaching product we used[2] (Whiteness HP Maxx, FGM Dental Products, Joinville, Santa Catarina, Brazil). To detect a reduction of TS of 50 percent, with a two-sided 5 percent significance level and a power of 80 percent, we determined that a minimal sample size of 20 participants per group was necessary, given a dropout rate of 5 percent.

Study design. We randomly divided the participants into the CF and CC hydrogen peroxide gel groups by means of a coin toss. To guarantee equal sample size, we ensured that participants always came to the bleaching session in pairs and that the coin was tossed just once to define the group to which one of the participants would be allocated. The other participant then was allocated to the other group. The decision

ABBREVIATION KEY. CC: Calcium containing. **CF:** Calcium free. **SGUs:** Shade guide units. **TS:** Tooth sensitivity.

regarding which participant was going to toss the coin was reached by agreement between them. After the prophylaxis procedures, the clinician (G.M.) isolated the gingival tissue of the teeth to be bleached by using a light-cured resin dam (Top Dam, FGM Dental Products). Two undergraduate students using calibrated technique used 35 percent CF hydrogen peroxide gel (Whiteness HP Maxx) and 35 percent CC hydrogen peroxide gel (Whiteness HP Blue, FGM Dental Products) according to the manufacturer's instructions (Table 1). The operators, who were not masked as to the procedure, performed two bleaching sessions with a one-week interval between sessions. We instructed all participants to brush their teeth regularly, at least twice per day, with fluoridated toothpaste (Sorriso Fresh, Colgate-Palmolive, São Paulo, Brazil) that we provided. The operators who performed the bleaching were not the same as those who assessed the color (S.K. and A.R.); the latter were masked as to the experimental conditions.

TABLE 1

Bleaching products, composition and application regimens.

PRODUCT	BRAND NAME (MANUFACTURER)	COMPOSITION	APPLICATION REGIMEN
Calcium Free	Whiteness HP Maxx 35% (FGM Dental Products, Joinville, Santa Catarina, Brazil)	35 percent hydrogen peroxide, thickeners, dye mixture, glycol, inorganic load, deionized water	• For the bleaching of each arch, mix 12 drops of phase 1 (hydrogen peroxide) with four drops of phase 2 (thickener) • Apply a thin layer of gel, approximately 0.5 mm thick, on the buccal surface of all teeth undergoing treatment • Leave the bleaching gel on the tooth surface for 15 minutes and then remove it with an aspirator • Repeat this procedure three times in each appointment
Calcium Containing	Whiteness HP Blue 35% (FGM Dental Products)	35 percent hydrogen peroxide, thickeners, inert violet, neutralizing agent, calcium gluconate, glycol, deionized water	• Attach both syringes securely to each other • Mix the contents of both phases by pressing the plungers of the syringes alternatively in opposite directions up to eight times • Press entire mixed content into one of the syringes and apply the product to the tooth surface • Leave the bleaching gel on the tooth surface for 40 minutes and then remove it with an aspirator

Shade evaluation. Two examiners (S.K. and A.R.), who were masked as to the treatment allocation and who used calibrated techniques, assessed the color at baseline and one day after each of the bleaching sessions by using a Vita shade guide. The shade guide's 16 tabs were arranged from the highest (B1) to the lowest (C4) value (B1, A1, B2, D2, A2, C1, C2, D4, A3, D3, B3, A3.5, B4, C3, A4, C4). Although this scale is not linear in the truest sense, for the purpose of analysis we treated the changes as representing a continuous and approximately linear ranking. The measurement area of interest for shade matching was the middle one-third of the facial surface of the anterior teeth (the central incisors), according to American Dental Association[19] guidelines. As the recruitment of participants was performed in the university, which means the study population consisted of young adults, we rarely found a participant with color darker than A3.5.

Before the study began, the examiners evaluated the shade of the central incisors in approximately 10 participants by using the Vita shade guide and discussed the cases in which their evaluations disagreed. Then they repeated this procedure independently in another 10 participants to determine the interexaminer agreement. We required that the two examiners have an agreement of at least 85 percent (weighted κ statistic) before beginning the study evaluation.

Participants' TS evaluation. The participants recorded their spontaneous perception of TS after bleaching. They used the following scale: 0, none; 1, mild; 2, moderate; 3, considerable; and 4, severe.

Statistical analysis. The analysis followed the intention-to-treat protocol and involved all participants. We calculated the means and standard deviations of shade guide units (SGUs) as recorded at baseline and after the first and second bleaching sessions. We evaluated the bleaching effectiveness of each group at each session's recall visit by means of the Friedman test, and we compared the groups (CC and CF) at each session's recall visit by means of the Mann-Whitney test ($\alpha = .05$). For each participant, we recorded a TS score after each bleaching, for a total of two scores per participant. We selected for statistical analysis only the worst score for each participant at

TABLE 2

Tooth shade according to the shade guide at each assessment point for the two treatment groups.

ASSESSMENT POINT*	TOOTH SHADE, IN SHADE GUIDE UNITS, ACCORDING TO TREATMENT GROUP†			
	Calcium Free		Calcium Containing	
	Mean (SD‡)	Median (interquartile range)	Mean (SD)	Median (interquartile range)
Baseline	9.1 (1.6)	9.5 (9–10.25)^{aA}	9.6 (1.4)	9 (8.75-9)^{aA}
After One Week	4.3 (1.5)	5 (3–5)^{bA}	4.7 (1.5)	5 (4-5.25)^{bA}
After Two Weeks	1.8 (0.6)	2 (1-2)^{cA}	1.4 (0.7)	1 (1-2)^{cA}

* At each assessment point, the groups were compared by means of a Mann-Whitney test; comparisons are represented by uppercase letters. Same uppercase letters indicate no statistically significant differences across rows ($\alpha = .05$).
† In each group, the different times were compared by means of the Friedman test; comparisons are represented by lowercase letters. Same lowercase letters indicate no statistically significant differences within columns ($\alpha = .05$).
‡ SD: Standard deviation.

TABLE 3

Participants' experience of tooth sensitivity during the bleaching regimen, as well as absolute and relative risks of experiencing sensitivity.

BLEACHING REGIMEN	PARTICIPANTS' EXPERIENCE OF TOOTH SENSITIVITY, NO.*		ABSOLUTE RISK, PERCENTAGE (95 PERCENT CI†)	RELATIVE RISK, PERCENTAGE (95 PERCENT CI)
	Yes	No		
Calcium Free	16	4	80 (58-92)	0.50 (0.28-0.89)
Calcium Containing	8	12	40 (22-61)	

* According to Fisher exact test ($P = .02$).
† CI: Confidence interval.

TABLE 4

Means and medians of participants' tooth sensitivity intensity scores for each bleaching regimen.*

BLEACHING REGIMEN	MEAN	MEDIAN (MINIMUM/MAXIMUM)	*P* VALUE†
Calcium Free	1.85	2 (0/3)	< .01
Calcium Containing	0.55	0 (0/3)	

* Values taken from participants' recording of tooth sensitivity on a scale from 0 to 4 after bleaching, with 0 meaning none; 1, mild; 2, moderate; 3, considerable; 4, severe.
† According to the Mann-Whitney test.

each measurement point. We evaluated the overall percentage (absolute risk) of participants who experienced TS at least once during the procedure (primary outcome) by means of the Fisher exact test ($\alpha = .05$) and evaluated overall TS intensity by means of the Mann-Whitney test ($\alpha = .05$). We calculated the relative risk as well as the confidence interval (CI) for the correct effect size.

RESULTS

All of the 40 participants who began the study completed it. A total of 28 women underwent bleaching, 13 in the CC group and 15 in the CF group. Most of the participants selected were university students and, therefore, were young, ranging in age from 18 to 30 years, with a mean (standard deviation [SD]) age of 22 (3) and 23 (3) years for the CC and CF groups, respectively. According to κ statistics, the level of agreement between the two evaluators was 87 percent. Table 2 shows the means and standard deviations and the medians of SGUs. The median tooth color at baseline was similar for the two groups ($P > .05$). Both materials bleached teeth at the same rate regardless of the bleaching session ($P > .05$). After two bleaching sessions, for both groups, there was a significant change in tooth shade of approximately 7 to 8 SGUs ($P < .05$) (Table 2). There was no difference in the final shade between the two groups.

With regard to the absolute risk of TS, the CF product had a significantly statistically higher ($P = .02$) prevalence of TS (80 percent) than did the CC product (40 percent) (Table 3). The risk of having TS was reduced 50 percent (95 percent CI, 28-89 percent) with the use of the CC bleaching gel. Table 4 and the figure summarize the level of TS for both groups; we detected sta-

tistically significant differences between them (Table 4). Whereas 90 percent of the participants in the CC group reported experiencing no or mild TS, only 30 percent of those in the CF group reported experiencing no or mild TS (Figure).

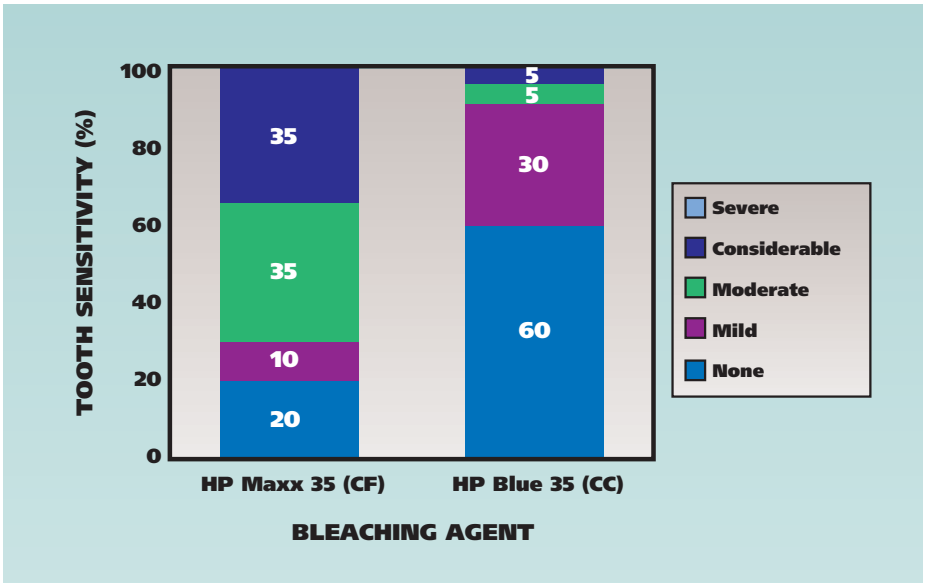

Figure. Levels of tooth sensitivity (percentage) that participants in each group perceived immediately after undergoing the bleaching protocol. CC: Calcium containing. CF: Calcium free. The bleaching agents were manufactured by FGM Dental Products, Joinville, Santa Carina, Brazil.

DISCUSSION

The results of this study indicate that both CF and CC products produced equivalent and significant tooth color enhancement as compared with baseline values (Table 2). Regarding bleaching effectiveness, both materials bleached teeth at the same rate after two bleaching sessions. Comparing color change after in-office bleaching with that in the literature is difficult, owing to investigators' use of different methods of measurement (shade guides and spectrophotometers) and different units of measurement (such as the Commission Internationale de L'Eclairage system and SGUs). However, investigators in studies involving the use of 35 percent hydrogen peroxide (with and without light activation) and the reporting of results in SGUs usually observed an overall color change of 5 to 8 SGUs after two bleaching sessions,[2,20-23] which finding is in agreement with our results. This wide range of color change probably is the result of the different materials used and also of the length of postbleaching time after which we assessed the color.

TS caused by in-office bleaching is by far the most undesirable adverse effect of this clinical procedure.[1] Some investigators have suggested that oxygen bubbles form in the dentinal tubules during hydrogen peroxide application and that these small pockets of gas cause dentinal fluid movements that activate the intradentinal nerves.[24] However, another theory suggests that the cause of TS is that oxygen released from the bleaching agent is capable of diffusing through the enamel and dentin and of causing noticeable damage to the pulp tissue.[5]

A closer analysis of clinical studies in which investigators performed in-office bleaching with 35 percent hydrogen peroxide reveals that the absolute risk of TS varies considerably across studies, ranging from 67 to 87 percent.[2-4,23,25] This contrast also was evident in our investigation. Participants in the CC group had not only a statistically lower absolute risk of TS than that in the CF group, but also a statistically lower TS intensity. When present in the CC group, the TS intensity generally was mild, which is different from what we observed in the CF group. This highlights the possibility that other components apart from the 35 percent hydrogen peroxide may cause or prevent TS.

One of the main differences between the two products we used in this study is that the CC product contains 2 percent calcium gluconate, which physicians have used extensively for treating hypocalcemia.[26] The application of bleaching agents to enamel may increase the porosity of this highly mineralized dental tissue owing to the agents' disruption of matrix protein, which causes loss of structural components by means of free radical oxidation.[27] These alterations include increased porosity, pitting, erosion and demineralization of enamel prisms' periphery,[28] which seems to alter the bleached enamel's microhardness.[16-18] This finding led some manufacturers to include 2 percent calcium gluconate in their bleaching gel formulation. Although the calcium was not added to reduce TS but to prevent enamel demineralization, we cannot rule out the possibility that this addition might have played a role in the lesser TS reported with use of the CC product. Perhaps the 2 percent of calcium gluconate dis-

solved into the hydrogen peroxide gel was able to decrease dentinal permeability and block enamel surface defects, similarly to what is believed to occur with bleaching gels containing amorphous calcium phosphate.[10,14] This hypothesis could explain the absence of this adverse effect in 60 percent of the participants treated with the CC product in this study (Table 3). However, we did not make any attempt to test whether calcium from the CC product formulation actually was available for reaction with the dental structure and not linked to other compounds. This issue still requires further investigation.

Another advantage of the CC product is that it maintains a high stable pH of 8 or 9 throughout the bleaching procedure, contrary to what occurs with CF gel (pH = 6 to 7). We confirmed these values in our laboratory by measuring the products' pH (A. Reis, DDS, PhD, unpublished data, January 2010). According to Price and colleagues,[29] whitening products should have a relatively neutral pH to minimize potential damage, but investigators have reported a pH variation of 2.4 to 6.53 for in-office bleaching gels.[29,30] This variation could be the result of the different formulations used by each manufacturer, because bleaching agents contain stabilizers and other inorganic components that allow them to be stored for prolonged periods. As noted earlier, most in-office bleaching gels are delivered in low pH because they are more stable in acid solutions than in base solutions. When hydrogen peroxide is to be stored, weak acid usually is added to the solution to prevent it from decomposing.[31]

The decomposition kinetics and the by-products produced by hydrogen peroxide depend on the pH of the medium in which it is stored. While it is in an acidic solution, oxygen free radicals and hydroxyl anions are produced, but an alkaline solution has a higher concentration of perhydroxyl ions.[32] Unfortunately, little is known about the deleterious effects of these different oxidizing agents on the dental-pulp complex.

Some investigators have reported that the hydrogen peroxide delivered in an alkaline medium increases the effectiveness of bleaching in the wool industry.[33] This effectiveness is explained by the fact that the dissociation constant of the hydrogen peroxide is about 11.5. In fact, the findings of one study showed that in a pH of 9, the dissociation rate of the hydrogen peroxide was 2.7 times higher than that in an acidic solution (pH = 4.4).[34] These variations, however, did not seem to produce differences in tooth bleaching effectiveness when we compared the two products in our study. Investigators should conduct further studies to elucidate whether these effects have any correlation with the lesser TS we have reported here for the CC product.

Investigators in ongoing studies are seeking other clinical alternatives, such as the use of selective cyclooxygenase-2 anti-inflammatory drugs before the bleaching procedure, to minimize or even prevent the undesirable effect of TS resulting from in-office bleaching. We also encourage investigation of the inflammatory mediators involved in the TS produced by tooth bleaching.

Finally, we should point out the limitations of this investigation. To guarantee groups with equal sample size, we scheduled participants in pairs in the strict sequence in which they entered the trial. We tossed the coin only once to determine the group assignment of one participant in each pair, and we automatically assigned the other participant to the other group. This procedure did not truly allocate all participants and, as such, may raise concerns with respect to the distribution of unknown risk factors at baseline. However, as we excluded potential participants who had prior tooth sensitivity, it is likely the two study groups were comparable at baseline.

CONCLUSION

It is likely that the addition of calcium gluconate and the stable and high pH of the CC product were responsible for the reduced TS reported by participants receiving this bleaching agent in our study. The CC hydrogen peroxide gel caused less TS during in-office dental bleaching without any deleterious effects on bleaching effectiveness. ■

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1. Haywood VB. Treating sensitivity during tooth whitening. Compend Contin Educ Dent 2005;26(9 suppl 3):11-20.
2. Tay LY, Kose C, Loguercio AD, Reis A. Assessing the effect of a desensitizing agent used before in-office tooth bleaching. JADA 2009;140(10):1245-1251.
3. Alomari Q, El Daraa E. A randomized clinical trial of in-office dental bleaching with or without light activation. J Contemp Dent Pract 2010;11(1):E017-E024.
4. Tang B, Millar BJ. Effect of chewing gum on tooth sensitivity following whitening (published online ahead of print May 28, 2010). Br Dent J 2010;208(12):571-577. doi:10.1038/sj.bdj.2010.500.
5. Costa CA, Riehl H, Kina JF, Sacono NT, Hebling J. Human pulp responses to in-office tooth bleaching. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;109(4):e59-e64.
6. Caviedes-Bucheli J, Ariza-García G, Restrepo-Méndez S, Ríos-

Osorio N, Lombana N, Muñoz HR. The effect of tooth bleaching on substance P expression in human dental pulp (published online ahead of print Oct. 31, 2008). J Endod 2008;34(12):1462-1465. doi:10.1016/j.joen.2008.09.013.

7. Caviedes-Bucheli J, Lombana N, Azuero-Holguín MM, Munoz HR. Quantification of neuropeptides (calcitonin gene-related peptide, substance P, neurokinin A, neuropeptide Y and vasoactive intestinal polypeptide) expressed in healthy and inflamed human dental pulp. Int Endod J 2006;39(5):394-400.

8. Leonard RH Jr, Smith LR, Garland GE, Caplan DJ. Desensitizing agent efficacy during whitening in an at-risk population. J Esthet Restor Dent 2004;16(1):49-55.

9. Armênio RV, Fitarelli F, Armênio MF, Demarco FF, Reis A, Loguercio AD. The effect of fluoride gel use on bleaching sensitivity: a double-blind randomized controlled clinical trial. JADA 2008; 139(5):592-597.

10. Matis BA, Cochran MA, Eckert GJ, Matis JI. In vivo study of two carbamide peroxide gels with different desensitizing agents. Oper Dent 2007;32(6):549-555.

11. Browning WD, Chan DC, Myers ML, Brackett WW, Brackett MG, Pashley DH. Comparison of traditional and low sensitivity whiteners. Oper Dent 2008;33(4):379-385.

12. Gallo JR, Burgess JO, Ripps AH, Bell MJ, Mercante DE, Davidson JM. Evaluation of 30% carbamide peroxide at-home bleaching gels with and without potassium nitrate: a pilot study. Quintessence Int 2009;40(4):e1-e6.

13. Yengopal V, Mickenautsch S. Caries preventive effect of casein phosphopeptide-amorphous calcium phosphate (CPP-ACP): a meta-analysis. Acta Odontol Scand 2009;67(6):321-332.

14. Giniger M, Macdonald J, Ziemba S, Felix H. The clinical performance of professionally dispensed bleaching gel with added amorphous calcium phosphate. JADA 2005;136(3):383-392.

15. Kanca J III. Bleaching gel with ACP (letter to the editor). JADA 2005;136(9):1214, 1216; author reply 1216, 1218.

16. de Oliveira R, Paes Leme AF, Giannini M. Effect of a carbamide peroxide bleaching gel containing calcium or fluoride on human enamel surface microhardness. Braz Dent J 2005;16(2): 103-106.

17. Borges AB, Samezima LY, Fonseca LP, Yui KC, Borges AL, Torres CR. Influence of potentially remineralizing agents on bleached enamel microhardness. Oper Dent 2009;34(5):593-597.

18. Cavalli V, Rodrigues LK, Paes-Leme AF, et al. Effects of bleaching agents containing fluoride and calcium on human enamel. Quintessence Int 2010;41(8):e157-e165.

19. American Dental Association, Council on Dental Therapeutics. Guidelines for the acceptance of peroxide-containing oral hygiene products. JADA 1994;1258:1140-1142.

20. Marson FC, Sensi LG, Vieira LC, Araújo E. Clinical evaluation of in-office dental bleaching treatments with and without the use of light-activation sources. Oper Dent 2008;33(1):15-22.

21. Bernardon JK, Sartori N, Ballarin A, Perdigão J, Lopes GC, Baratieri LN. Clinical performance of vital bleaching techniques. Oper Dent 2010;35(1):3-10.

22. Strobl A, Gutknecht N, Franzen R, Hilgers RD, Lampert F, Meister J. Laser-assisted in-office bleaching using a neodymium: yttrium-aluminum-garnet laser: an in vivo study (published online ahead of print May 9, 2009). Lasers Med Sci 2010;25(4):503-509. doi:10.1007/s10103-009-0675-2.

23. Reis A, Dalanhol AP, Cunha TS, Kossatz S, Loguercio AD. Assessment of tooth sensitivity using a desensitizer before light-activated bleaching (published online ahead of print March 24, 2011). Oper Dent 2011;36(1):12-17. doi:10.2341/10-148-CR.

24. Markowitz K. Pretty painful: why does tooth bleaching hurt? (published online ahead of print Dec. 31, 2009). Med Hypotheses 2010;74(5):835-840. doi:10.1016/j.mehy.2009.11.044.

25. Nathanson D, Parra C. Bleaching vital teeth: a review and clinical study. Compendium 1987;8(7):490-497.

26. Broner CW, Stidham GL, Westenkirchner DF, Watson DC. A prospective, randomized, double-blind comparison of calcium chloride and calcium gluconate therapies for hypocalcemia in critically ill children. J Pediatr 1990;117(6):986-989.

27. Kwon YH, Huo MS, Kim KH, Kim SK, Kim YJ. Effects of hydrogen peroxide on the light reflectance and morphology of bovine enamel. J Oral Rehabil 2002;29(5):473-477.

28. Akal N, Over H, Olmez A, Bodur H. Effects of carbamide peroxide containing bleaching agents on the morphology and subsurface hardness of enamel. J Clin Pediatric Dent 2001;25(4):293-296.

29. Price RB, Sedarous M, Hiltz GS. The pH of tooth-whitening products. J Can Dent Assoc 2000;66(8):421-426.

30. Freire A, Archegas LR, de Souza EM, Vieira S. Effect of storage temperature on pH of in-office and at-home dental bleaching agents. Acta Odontol Latinoam 2009;22(1):27-31.

31. Chen JH, Xu JW, Shing CX. Decomposition rate of hydrogen peroxide bleaching agents under various chemical and physical conditions. J Prosthet Dent 1993;69(1):46-48.

32. Sun G. The role of lasers in cosmetic dentistry. Dent Clin North Am 2000;44(4):831-850.

33. Trotman ER. Dyeing and Chemical Technology of Textile Fibres. 6th ed. New York City: John Wiley & Sons; 1985:587.

34. Frysh H, Bowles WH, Baker F, Rivera-Hidalgo F, Guillen G. Effect of pH on hydrogen peroxide bleaching agents. J Esthet Dent 1995;7(3):130-133.