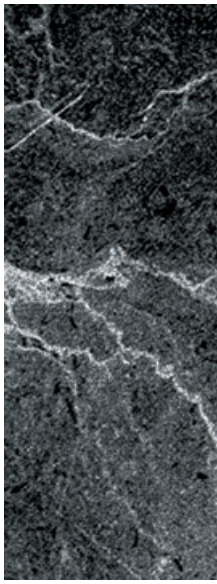

Critical Appraisal

COMPARISON OF THE EFFECTIVENESS AND SAFETY OF CARBAMIDE PEROXIDE WHITENING AGENTS AT DIFFERENT CONCENTRATIONS

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In today's society, it seems everything needs to be faster. As a result some practitioners are using whitening products with higher concentrations of the active ingredient in an attempt to provide faster whitening. Do they whiten faster, and if so, does it result in more sensitivity? This article reviews four studies to explore these two questions.

A CLINICAL EVALUATION OF 10 PERCENT VS. 15 PERCENT CARBAMIDE PEROXIDE TOOTH-WHITENING AGENTS

P.W. Kihn, D.M. Barnes, E. Romberg, K. Peterson
Journal of the American Dental Association 2000 (131:1478–84)

ABSTRACT

Objective: To determine whether a 15% carbamide peroxide (CP) whitening agent whitens teeth to a greater extent than a 10% agent. In addition, tooth sensitivity was assessed and compared to evaluate whether the higher-concentration CP worsened side effects.

Materials and Methods: Two concentrations of the NUPRO Gold Tooth Whitening System (Dentsply Preventive Care, York, PA, USA) were compared in a double-blind clinical trial involving 56 human subjects matched into 28 pairs. Bleaching stents were fabricated using the manufacturer's suggested materials and techniques, and participants used their assigned material according to the manufacturer's instructions. Extrinsic stains were removed prior to the start of the study, and the baseline color was measured using a value-ordered Vita Classic shade guide (VITA, Bad Säckingen, Germany). Active

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treatment was for 2 weeks. In addition to the baseline shade, color was assessed after 1 and 2 weeks of treatment, and 2 weeks following the end of treatment.

Each person recorded tooth sensitivity daily using a 20-mm visual analog scale. Participants marked their pain level with a hash mark anywhere along the line that represented what he or she felt.

Results: One person experienced extreme sensitivity and, along with the matching participant, was dropped from the study after 2 days. Another participant was dropped because of noncompliance with the use of the gel. Again, both participants in the pair were dropped. Fifty-two people, or 26 pairs, completed the trial. The pain levels for the participant who dropped out because of sensitivity were not included in any analysis, and there was no report regarding the agent to which he or she was assigned. There was a significant efficacy difference in the two groups at the end of active treatment and at the 2-week post-treatment evaluation. The 15% product was associated with significantly more color change than the 10% product. The means (and SDs) were 9.4 (2.3) and 7.7 (3.0) tabs, respectively.

On a scale of zero to 20, the means (and SDs) for the sensitivity scores were 4.2 (4.6) and 2.8 (2.4) for the 15 and 10% groups, respectively. The difference in sensitivity score was not significant. However, the authors did note that the variability in sensitivity scores, as measured by the SD, was significantly different for the two groups.

Conclusions: While the 15% CP product did not significantly increase the whitening effect observed after 1 week of treatment, it did after 2 weeks of treatment and at 2 weeks post-treatment. There was no significant difference in sensitivity between the two groups.

COMMENTARY

The mean sensitivity score for the 15% CP group was approximately 1.5 times greater than that of the 10% group, yet the difference was not statistically significant. Because the sample sizes, means, and SDs for both groups were included in the publication, it was possible to reanalyze the data to calculate the statistical power or the ability to find a significant difference, if one existed. In reanalyzing the data, it was possible to determine that the statistical power for that comparison was 0.15. The accepted standard is 0.80. Probably resulting from the variability in responses from participant to participant, this study simply did not include enough participants to find a statistical difference, even if one existed.

This article is often cited to support the idea that whitening with 15% CP is more efficient or produces a better result in the same amount of time. The results at the end of active treatment and 2 weeks following treatment do support the conclusion that the 15% CP produced a better result.

However, the choice to wait only 2 weeks following the end of active treatment to perform the final color evaluation is highly problematic. The whitening effect is known to relapse or rebound shortly after cessation of active bleaching. It is believed that part of the color change is temporary and the result of dehydration of the teeth during active bleaching. Only after the teeth have rehydrated can one assess the real color change. Subsequent studies (see articles noted below) have demonstrated that, whereas teeth whitened with 10% CP have stabilized in color 2 weeks following the end of active treatment, higher-concentration products take much longer. Accordingly, the significant color difference observed at the end of the study is very likely a result of incomplete stabilization of the color change.

CLINICAL EVALUATION OF BLEACHING AGENTS OF DIFFERENT CONCENTRATIONS

B.A. Matis, H.N. Mousa, M.A. Cochran, G.J. Eckert
Quintessence International 2000 (31:303–10)

ABSTRACT

Objective: This study compared the tooth whitening efficacy of two CP products with different concentrations of the active ingredient. The products were Opalescence 10% and Opalescence F 15% (Ultradent Products, Inc., South Jordan, UT, USA). In addition, color rebound and gingival and tooth sensitivity were compared.

Materials and Methods: This was a randomized, double-blind clinical trial using a split-mouth design. Twenty-five participants were randomly assigned to receive one material on the right and the other on the left side. Extrinsic stains were removed before the start of the study. Active bleaching was for 2 weeks.

Color change was measured three ways: first, L^*, a^*, and b^* data were recorded using a colorimeter (Chroma Meter CR-321, Minolta, Ramsey, NJ, USA). The colorimeter positioning was standardized from evaluation to evaluation using a custom-fabricated jig. Second, shade tab change was measured using a value-ordered shade guide (Bioform, Dentsply Trubyte, York, PA, USA). Third, color differences between the right and left sides were measured using color photos. Potential differences between the right and left sides were rated on a 4-point categorical scale. Color was evaluated at baseline, 3 days, and 1 and 2 weeks during active treatment. Postbleaching color evaluations were conducted at 3 and 6 weeks or 1 and 4 weeks post-treatment.

Opalescence F 15% contained fluoride for the purpose of reducing sensitivity, whereas Opalescence 10% did not. Participants recorded gingival and tooth sensitivity separately on a daily basis using a 5-point categorical scale. However, subjects who experienced sensitivity levels greater than 3 were provided a 3% potassium nitrate desensitizing gel rather than their active bleaching agent. Any night that the desensitizing gel was substituted for the active treatment was not counted as a night of active bleaching.

Results: Colorimeter data indicated significant differences between groups at 1, 2, and 3 weeks, but not at the final evaluation. This was true for ΔE, ΔL^*, Δa^*, and Δb^*.

The shade guide data also noted significant differences between the groups for all evaluations except the final evaluation. The photographic comparisons of the two sides found no significant difference between the groups at the final evaluation.

There was a clear trend for tooth sensitivity to be greater in the 15% CP group, but the difference was not significant. The same held true for gingival sensitivity.

Conclusions: Practitioners should inform patients that the lighter shade obtained with 15% CP used for the same amount of time as 10% CP is temporary.

COMMENTARY

Similar to the Kihn et al. study, this study found significant color change differences between the groups after 2 weeks of active treatment and at 2 weeks or less following the end of active bleaching. Unlike the Kihn et al. study, this study also found a significant difference in color between the two groups after 1 week of bleaching. More importantly, this study scheduled the final color evaluation more than 2 weeks after the cessation of bleaching. This allowed for more color relapse or rebound to occur before making a final color assessment than in the Kihn et al. study.

The colorimeter data indicate that both groups showed rapid rates of

relapse in color between the 2- and 3-week evaluations. From the 3- to the 6-week evaluation, the 10% group did not relapse further in terms of ΔL^* and Δb^*. In contrast, the 15% CP group continued to relapse in terms of ΔE, ΔL^*, Δa^*, and Δb^*. These results emphasize the need for the postbleaching evaluation to occur *after* the color change has had a chance to stabilize. It also provides evidence that the time required for color stabilization is longer for products with a higher percentage of the active ingredient.

The 15% CP product contained an ingredient to reduce sensitivity, whereas the 10% CP product did not. To what extent the inclusion of this ingredient affected the results is unknown. For those participants who reported levels of sensitivity of 3 or higher, a desensitizing agent was provided. This was included to protect the participants. Although this was ethically required, one still must be aware that the use of the desensitizing agent would cause the study to underestimate sensitivity levels.

As with the Kihn et al. study, the data demonstrated a clear trend for lower tooth sensitivity in the 10% CP group, but the difference was not statistically significant. This study did not publish detailed data regarding sensitivity. Rather, just the results of the testing were reported. Accordingly, it was not possible to determine the statistical power of this study. It can be noted, however, that, relative to the Kihn et al. study, the present study included 25 rather than 52 subjects, and the appropriate statistical test used for the sensitivity comparison was nonparametric rather than parametric. Both of these factors, generally speaking, would provide less statistical power rather than more.

COMPARATIVE SEVEN-DAY CLINICAL EVALUATION OF TWO TOOTH WHITENING PRODUCTS

S. Nathoo, E. Santana III, Y.P. Zhang, N. Lin, M. Collins, K. Klimpel, W. DeVizio, M. Giniger
Compendium of Continuing Education in Dentistry 2001 (22:599–606)

ABSTRACT

Objective: This study compared the tooth whitening efficacy of two carbamide peroxide products. The products were Colgate Platinum Gentle Plus (Colgate Oral Pharmaceuticals, New York, NY, USA), with 5% CP, and Nite White Excel 2Z (Discus Dental, Culver City, CA, USA), with 10% CP. In addition, tooth sensitivity was compared between the two groups.

Materials and Methods: This was a randomized, double-blind clinical trial involving 60 participants. Active bleaching was for 1 week, with participants using the whitening agents 6 to 8 hours per night. Bleaching stents were fabricated using the materials and techniques recommended by each manufacturer. Extrinsic stains were removed before the start of the study. Color measurements were made at baseline, 3, 5, and 7 days using a value-ordered shade guide (Vita Classic). Color measurements were also made with a colorimeter (Chroma Meter CR-321) at baseline and 7 days. A positioning jig was fabricated for each participant to assure consistent positioning. Participants were questioned as to whether they experienced tooth sensitivity at any point during the week. Responses were limited to yes and no. Both products included potassium nitrate, which is intended to reduce sensitivity.

Results: Mean shade guide data were compared at 3, 5, and 7 days. Colorimeter data were used to calculate overall color change, ΔE. The mean ΔE for the two groups was compared at 7 days. In terms of tooth whitening efficacy, there

were no significant differences between the two groups at any evaluation period. One participant in the 10% CP group withdrew because of extreme tooth sensitivity, and 53% of participants reported sensitivity at some time. For the 5% CP group, 20% of participants reported sensitivity. The difference was statistically significant.

Conclusions: The 5% CP whitening agent was associated with equivalent whitening and significantly less tooth sensitivity.

COMMENTARY

The results of this study agree with the Kihn et al. study and disagree with the results of the Matis et al. study in that the 10% product did not produce more whitening than the 5% product within the first week. Because no postbleaching evaluations were scheduled, this study does not provide any information about the overall color change achieved or the degree of rebound experienced by either agent.

Similar to the two previous studies, the trend in this study was for more tooth sensitivity to be associated with the higher-concentration product. Unlike the previous studies, this study noted only the percentage of participants who experienced tooth sensitivity at some time during the study rather than the participants' levels of pain. Accordingly, this study does not contribute any information about the duration or severity of that sensitivity. But the difference between the groups was significant, which indicates that, regardless of severity, more participants in the 10% CP group experienced tooth sensitivity.

EXTENDED AT-HOME BLEACHING OF TETRACYCLINE-STAINED TEETH WITH DIFFERENT CONCENTRATIONS OF CARBAMIDE PEROXIDE

B.A. Matis, Y. Wang, T. Jiang, G.J. Eckert
Quintessence International 2002 (33:645–55)

ABSTRACT

Objective: This study compared the tooth whitening efficacy of three CP products in tetracycline-stained teeth. The three agents had different concentrations of active ingredient—10, 15, and 20% CP. In addition, color rebound and gingival and tooth sensitivity were compared.

Materials and Methods: This was a randomized, double-blind clinical trial using a split-mouth design. Only the percentage of CP was described for the three whitening agents used. Six groups encompassing all possible combinations of the three products and alternating each agent between both the right and left sides were created, and participants were randomly assigned to each.

Active bleaching was for 6 months, unless a participant achieved a satisfactory level of whitening at 3 months. In addition to baseline, color evaluations were performed at 1 week, 2 weeks, and 1, 2, 3, 4, 5, and 6 months during active bleaching. Color evaluations were also completed at 7, 8, and 9 months or 1, 2, and 3 months postbleaching.

Color was evaluated using the Vitalescence Esthetic Restorative Masters Shade Guide (Ultradent Products, Inc.), with shades C6, C7, C8, and C9 added. L^*, a^*, and b^* measurements were made for each shade tab in the system. Evaluators matched teeth using the shade guide, but the data used for analysis were the corresponding L^*, a^*, and b^* readings for the shade tab chosen. Using color photographs, two evaluators rated color differences between the right and left sides using a forced consensus model.

Participants recorded gingival and tooth sensitivity separately on a daily basis using a 5-point

categorical scale during active bleaching, and for 1 month following cessation of bleaching. The sensitivity data was combined into 4-week periods to simplify analysis. However, subjects who experienced sensitivity levels greater than 3 were provided a 3% potassium nitrate desensitizing gel rather than their active bleaching agent. If more than moderate sensitivity continued, the participant was placed on 10% CP instead of a higher concentration.

Results: Fifty-nine subjects were enrolled and completed the study. For the 10, 15, and 20% CP agents, the numbers of half-arches treated were 40, 39, and 39, respectively. While all three products demonstrated continuous lightening throughout the 24 weeks of the study, after 1 month of bleaching the 10, 15, and 20% concentrations had produced 54, 60, and 62% of their maximum lightening, respectively.

Comparing the right and left sides using the color photos, there were no color differences for the 10% CP versus the 15 and 20%, and for the 15 versus the 20% at the final evaluation. However, the 20% side was significantly brighter than the 10% side at 1 and 2 weeks. The 15% side was not brighter than the 10% side at any evaluation. Color change was stable at 1 and 2 months for the 15 and 10% agents, respectively. For the 20% agent, color had not stabilized at 3 months postbleaching.

Overall tooth sensitivity was significantly lower for the 10% group compared with both the 15 and 20% groups. There was no significant difference in tooth sensitivity levels for the 15 and 20% groups. The 20% product was associated with significantly higher gingival sensitivity than the 10 and 15% products.

During 6 months of active bleaching, 85% of participants using the 10% CP product experienced sensitivity at some point. For the 15 and 20% CP products, the sensitivity rate was 100%. For participants using 10% CP on one side and 20% CP on the other, 100% of complaints of sensitivity were about the 20% side.

Eight subjects requested changes in products after first trying to reduce sensitivity using the desensitizing gel. None who requested the change were using the 10% gel on the side that was troublesome.

Conclusions: Ten percent CP is as effective as the higher concentrations at bleaching tetracycline-stained teeth and causes less tooth sensitivity.

COMMENTARY

It is unclear which products were used and whether any or all of the agents contained desensitizing agents.

Color evaluation of tetracycline-stained teeth is very challenging. Accordingly, adding shades lower in value or darker than those typically included in shade guides is appropriate and understandable. However, the use of the Vitalescence shade guide to establish L^*, a^*, and b^* data is problematic. Historically, bleaching studies use a value-ordered shade guide to evaluate brightness only. The human eye is very capable of accurately perceiving brightness. Data are available to arrange several commercially available shade guides from darkest to lightest to create an imperfect, but useful, ordinal scale. Shade guides have a major advantage in that they quantify the change in brightness in a way that is clinically meaningful to dentists and patients. Finally, one must be mindful that, if a study finds a statistically significant difference between products but that difference is not perceptible to the eye, the results are clinically irrelevant.

The shade guide created by the authors is clearly arranged by brightness. However, in terms of a^* and, especially, b^*, the tabs are not clearly aligned from more red to more green and more yellow to more blue, respectively. Accordingly, using the L^* reading for the corresponding shade tab might be

appropriate, but it is hard to justify assigning the corresponding *a** and *b** readings. Considering two teeth with the same level of brightness, one tooth might be yellow-red in hue and the other gray-brown. For the shade guide arrangement used, there is a single tab that matches these teeth for brightness. But there are not several tabs with the same level of brightness, some of which are yellow-red and some of which are gray-brown. Using the same *a** and *b** readings for these two teeth would be inaccurate. Finally, the authors neither report data nor cite other studies that can establish this shade guide as valid and reliable for this purpose. Accordingly, the consensus using photographs to compare the brightness of the right and left sides is probably a more reliable measure of efficacy.

This study supports the conclusion that, initially, the whitening process exhibits a dose and time response, with the higher-concentration product yielding a significantly better result. It is also clear that there is some unknown limiting factor within the tooth. As a result, the initial advantage of the higher-concentration products is quickly negated, and after the color change has stabilized, there is no difference between products. This is further supported by the fact that, for all three products, 54 to 62% of the whitening benefit occurred in the first 17% of the active treatment schedule. Furthermore, increasing the concentration of the active ingredient and the length of treatment appears to increase the amount of time required for the color change to stabilize.

A desensitizing agent was offered for all participants experiencing more-than-moderate sensitivity. In addition, participants with prolonged, moderate sensitivity were switched to a lower-concentration product. Both of these steps were included to protect participants, an essential aspect of any study involving human subjects. However, both factors would cause the study to tend toward underestimating sensitivity levels, especially in the higher-concentration products. The results of this study are consistent with that seen in the other studies discussed. The trend is for higher-concentration agents to be associated with more tooth sensitivity. Because this study involves more half-arches than the previous Matis et al. study, approximately 40 versus 25, and a longer active bleaching phase, more data points were created. Both of these issues result in increased statistical power. Unlike the Kihn et al. study and the first Matis et al. study cited, this study found a significant association between the percentage of active ingredient and tooth sensitivity. This is in agreement with the Nathoo et al. study. In addition, gingival sensitivity was significantly associated with the 20% CP product.

SUGGESTED READING

Braun A, Jepsen S, Krause F. Spectrophotometric and visual evaluation of vital tooth bleaching employing different carbamide peroxide concentrations. Dent Mater 2007;23:165–9.

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 2000;29(Suppl):S22–8.

Leonard RH, Garland GE, Eagle JC, Caplan DJ. Safety issues when using a 16% carbamide peroxide whitening solution. J Esthet Restor Dent 2002;14:358–67.

Ziebolz D, Helms K, Hannig C, Attin T. Efficacy and oral side effects of two highly concentrated tray-based bleaching systems. Clin Oral Investig 2007;11(3):267–75.

THE BOTTOM LINE

Taken as a whole, these four articles highlight three clear trends: first, if higher-concentration bleaching agents offer any efficacy advantage, it is only seen in the early stages of bleaching. In the two studies that included postbleaching color evaluations after the teeth had an adequate time for color rebound, at the final evaluation there was no significant difference in efficacy between lower- and higher-concentration products.

The study that involved a comparison between the 10 and 20% concentrations, especially dark teeth and an active phase of treatment 4 to 12 times longer than the norm, would seem to offer the best opportunity to find a clinically important difference in efficacy, if one actually existed. Yet trained examiners found no significant difference between the left and right sides of the mouth after the first 2 weeks.

Second, the data also indicate that higher-concentration products require longer time periods for color change to stabilize. The study involving 6 months of active treatment also offers some evidence that increasing the length of time that patients use the bleach increases the time required for color stabilization.

Third, higher-concentration bleaching agents are associated with more sensitivity. In both the Kihn et al. and the first Matis et al. study, the sensitivity data consistently trended higher for those using higher-concentration bleaching agents. The Kihn et al. study clearly lacked the statistical power to find a significant difference. It seems very likely that the first Matis et al. study did as well. The other two studies found significant differences between the lower-concentration products and the higher-concentration products in terms of sensitivity. For sensitivity data, statistical power is an issue because of the variability in response between one research participant and another. In the studies I have conducted, a majority of participants either had no sensitivity at any time or very mild sensitivity for a day or two. For the minority who did experience sensitivity, it was a very different experience. Reports of average sensitivity levels of 1.5 on a scale of 5 should be taken in this context. It is important to recall that the minority of subjects who experienced sensitivity had to balance out a lot of days of bleaching that rated scores of zero to get the average up even to 1.5.

In summary, the advantage of 15 and 20% bleaching agents over 10% products is that in the first week or two the patient's teeth will be slightly whiter. However, this difference will be temporary, and following rebound there will be no difference. The disadvantages are higher levels of sensitivity and a longer wait for the color to stabilize. The increased concern with color rebound means longer waits before additional cosmetic procedures can be initiated. The situation is further complicated if the color change that was acceptable to the patient at the end of treatment is no longer acceptable when the teeth have rebounded 1 to 3 months later. You and your patient are now facing several more weeks of waiting—weeks spent bleaching and waiting for the color to stabilize again.

Editor's Note: We welcome readers' suggestions for topics and contributors to Critical Appraisal. Please address your suggestions to the section editor:

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