Comparative Clinical Efficacy of Two Professional Bleaching Systems

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Abstract: ***A randomized, parallel, examiner-blind clinical trial was conducted to compare two professionally dispensed vital bleaching systems. A total of 20 subjects were randomized to either the Crest® Professional Whitestrips system or the Nite White® Excel 2 tray system, balancing for baseline tooth color. During the 2-week treatment period, subjects were instructed to use the strip system for one-half hour twice daily (14 contact hours) and the tray system for 2 hours daily (28 contact hours). Only the maxillary teeth were treated, and all bleaching was unsupervised. Whitening was measured objectively by comparing digital images of the maxillary anterior dentition at pretreatment and posttreatment. Compared with baseline, both the strip and tray systems exhibited statistically significant decreases ($P < 0.05$) in yellowness (Δb^*) and increases in brightness (ΔL^*). Compared with the tray-system group, the strip-system group experienced significant additional whitening ($P < 0.03$), as evidenced by a 62% to 209% improvement in tooth color (Δb^*, ΔL^*, and ΔE^*) after 14 days. Both systems were generally well tolerated, and none of the subjects discontinued treatment early because of an adverse event. Under the conditions tested, this clinical trial demonstrates that the 14-contact-hour treatment with the strip system resulted in superior whitening efficacy compared with the 28-contact-hour treatment with the tray system.***

Learning Objectives

After reading this article, the reader should be able to:

- compare the new whitening strip to a popular tray-based system.
- explain why an objective and quantitative method for measuring color change is useful in comparative clinical trials involving dissimilar products.
- discuss the role of compliance in clinical response to bleaching.

Vital tooth bleaching with peroxide is one of the most common cosmetic procedures in dentistry. Appearance may be improved by several "shades" with bleaching, depending on the peroxide concentration, its contact time with the target teeth, and other factors.[1] There are few contraindications to bleaching, and the primary adverse events—transient tooth sensitivity and gingival irritation—are typically mild in severity and resolve during treatment or immediately or shortly afterward.[2-4] Long-term follow-up suggests that the cosmetic benefit may be maintained for several years with no residual problems.[5]

A variety of professionally administered systems for in-office bleaching and professionally dispensed systems for at-home use are available. Of these, the at-home, custom tray-based systems are most common. Filled with bleaching gel, the custom trays can be worn for 2 or more hours daily for several days until desired whitening is achieved. Trade publications describe at least 16 different suppliers of at-home, tray-based bleaching systems.[6] These systems have varied peroxide concentrations, flavors, desensitizing agents, or other modifications to the formulation. To date, few of these formulations have been tested in adequate and well-controlled clinical trials and reported in peer-reviewed literature. Pending such research, some recommend that the 10% carbamide peroxide, tray-based system be considered a reference standard.[4]

The recently introduced whitening strip (Crest® Whitestrips[a]) is reported to represent a clear departure from conventional at-home bleaching systems.[7] This easy-to-use, hydrogen peroxide gel strip is reported to yield a similar response to a

[a] The Procter & Gamble Co, Cincinnati, OH 45202; 800-492-7378

Table 1—Treatment Groups and Regimen

Device	Gel Active	Quantity	Daily Contact Time	Brushing
Whitening strip	Hydrogen peroxide	28 Strips	30 Minutes twice daily	After bleaching
Custom tray	Carbamide peroxide + hydrogen peroxide	3 Syringes	2 Hours once daily	Before bleaching

marketed 10% carbamide peroxide tray-based system in half the contact time.[8] New clinical research was conducted to compare a higher-concentration whitening strip, containing 6.5% hydrogen peroxide in an aqueous gel, with a marketed 10% carbamide peroxide tray system.

Methods

The study population in this randomized, examiner-blind, clinical trial was healthy, employed adults who desired to have their teeth whitened. Although tooth color was not an entrance criterion, volunteers with a history of tooth bleaching, current tooth sensitivity, or facial anterior restorations were excluded from the study. After written and verbal informed consent was obtained, a thorough oral examination was performed. For balance and assignment purposes, tooth shade was measured in triplicate on the maxillary right central and lateral incisors using a chroma meter (ShadeEye-Ex[b]). Dental impressions of the maxillary arch were made on all subjects before randomization and treatment assignment.

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A single average shade score was constructed for each individual. Subjects were randomized in blocks of four, based on age and average estimated shade, to one of two professionally dispensed whitening systems:

- Strip system—Crest® Professional Whitestrips with 6.5% hydrogen peroxide.
- Tray system—Nite White® Excel 2[c] with carbamide and hydrogen peroxides, equivalent to 10% carbamide peroxide.

For the tray group only, a soft, full maxillary arch, custom bleaching tray was fabricated with gingival scalloping without reservoirs using materials supplied by the manufacturer. Approximately 5 days after the screening visit, all subjects returned for the baseline evaluation. Each custom-made bleaching tray was adjusted to ensure no gingival impingement. Subjects received their test products (bleaching strips or bleaching syringes and custom trays), and were instructed on product application and removal. Individuals assigned to the strip group were instructed to use the test strips twice daily for a total of 1 hour, while individuals in the tray group were instructed to wear the gel-loaded bleaching tray once daily for 2 hours (Table 1). In the strip group, subjects received 28 maxillary bleaching strips, each of which carried 0.2 g of the 6.5% hydrogen peroxide bleaching gel (a total of 5.6 g of bleaching gel). In the tray group, subjects received 3 bleaching syringes, each of which contained 4 g of the 10% carbamide peroxide-equivalent bleaching gel (a total of 12 g of bleaching gel). All subjects were supplied with an anticavity toothpaste (Crest® Cavity Protection Regular Paste[a]) containing 0.15% wt/vol ionic fluoride, and a soft toothbrush (Crest® Complete Extra Soft[a]) for use during the study. Participants returned on day 14 for the discharge oral examination and interview to elicit any symptoms experienced during the treatment period.

All test products were obtained from a single lot and stored under ambient conditions before dispensation. Test products were overlabeled with a uniquely numbered subject identification label and 24-hour contact number for use in case of an emergency. In addition to the test products, subjects received the manufacturer's supplied instructions for use. Because groups

[b] Shofu Dental Corp, Menlo Park, CA 94025; 650-324-0085
[c] Discus Dental, Inc, Culver City, CA 90232; 800-422-9448

differed as to the device and regimen, efficacy was measured using digital imaging analysis, an objective and quantitative method for color measurement that has been successfully used in partially blinded clinical trials to demonstrate a peroxide-dose relationship.[8] Digital images were collected at baseline and on day 14 of treatment using a standard method.

In brief, subjects were positioned in a chin rest and aligned, and then the facial anterior tooth surfaces were imaged under standard polarized lighting conditions using a high-resolution digital camera. Red-green-blue (RGB) values were determined for each tooth pixel with reference to a calibration standard, and these values were averaged across all 6 maxillary anterior teeth. RGB values were then transformed to derive numerical values for tooth color in terms of L*, a*, b*, which represent three-dimensional tooth color from light to dark, green to red, and blue to yellow, respectively.[9] Color change (ΔL*, Δa*, and Δb*) was determined by comparing each posttreatment visit to baseline. Negative Δb* (reduction in yellow) and positive ΔL* (increased brightness) were considered to be indicative of a whitening benefit. Using a standard method, a composite color score (ΔE*) was derived as the square root of the sum of the squares of the individual color changes. Between-group comparisons for Δb*, ΔL*, and ΔE* were made using analysis of covariance (ANCOVA), with the baseline value as the covariate. Comparisons to baseline were one-sided, while between-group comparisons were 2-sided at a 5% level of significance.

There are few contraindications to bleaching, and the primary adverse events—transient tooth sensitivity and gingival irritation—are typically mild in severity and resolve during treatment or immediately or shortly afterward.

Results

The 20 generally healthy adults ranged from 22 to 59 years of age. Of these, 55% were men, only 10% were current tobacco users, and

Table 2—Baseline Demographics and Tooth Color

Parameter	Strip Group (n = 10)	Tray Group (n = 10)	Two-sided *P*-value
Age (years)			
Mean (SD)	36.0 (11.05)	40.5 (10.88)	0.371
Minimum–maximum	22–49	24–59	
Gender			
Female	5 (50%)	4 (40%)	0.999
Male	5 (50%)	6 (60%)	
Ethnicity			
Nonwhite	2 (20%)	1 (10%)	0.999
White	8 (80%)	9 (90%)	
Tobacco, Coffee, and/or Tea Use			
Yes	9 (90%)	10 (100%)	0.999
Mean Tooth Color (SD)			
L*	74.86 (2.186)	73.59 (2.775)	0.270
a*	7.90 (0.639)	8.09 (0.892)	0.594
b*	18.70 (1.231)	19.15 (1.65)	0.497

SD = standard deviation

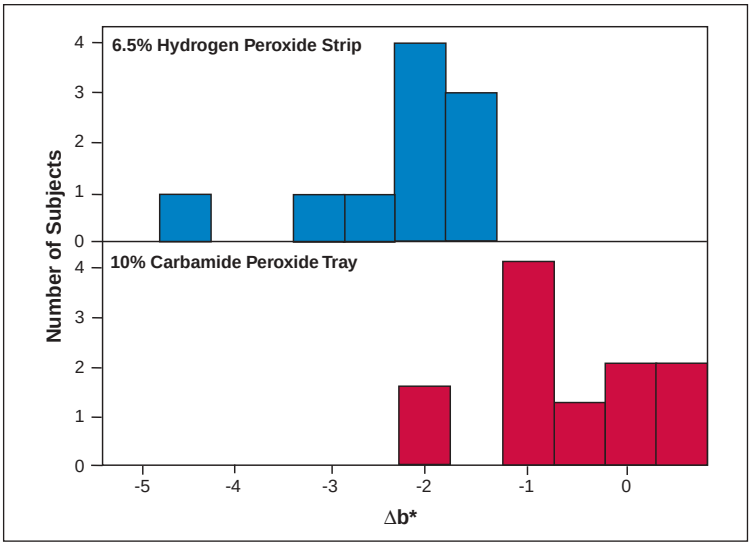

Figure 2—Distribution of change in brightness (ΔL*) tooth color.

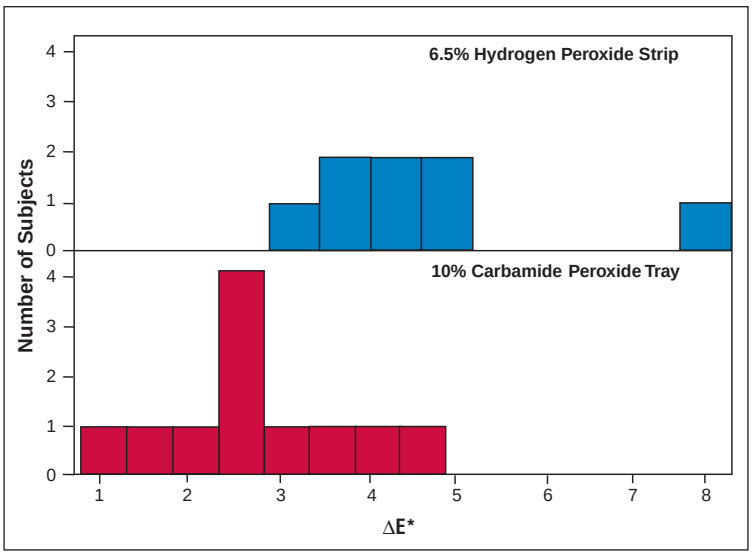

Figure 3—Distribution of change in composite (ΔE*) tooth color.

95% consumed coffee or tea daily. Treatment groups were balanced with respect to demographic characteristics and baseline tooth colors (Table 2). All 20 subjects completed the 14-day treatment and were considered eligible for evaluation for all analyses.

Both groups exhibited a statistically significant ($P < 0.05$) reduction in b*, which represents a shift from yellow to blue. In addition, both groups experienced significant increases in L* and E*, the other color parameters of interest, which provide evidence of increased brightness and overall color change relative to starting color. While both treatment groups experienced an overall improvement in color, the histograms demonstrate the considerable differences in clinical response between the treatment groups (Figures 1 through 3). For each of the color parameters Δb*, ΔL*, and ΔE*, the distribution was shifted toward greater whitening in the strip group relative to the tray group. (For Δb*, decreased values—more negative numbers—represent greater whitening.)

All subjects in the strip group experienced at least a 1-unit improvement for each color parameter evaluated (Δb*, ΔL*, and ΔE*). Outcomes in the tray group were generally favorable, though 60% of the subjects had relatively modest Δb* responses that were lower than a 1-unit change threshold. Only the strip group exhibited a significant change in red to green (Δa*) during treatment.

The histograms demonstrate the presence of 1 high responder, a 22-year-old, nonsmoking black man assigned to the strip group. The 14-day response in that individual was –4.40 and 6.20 for Δb* and ΔL*, respectively, which represented the greatest benefit in either treatment group. The clinical presentation was equally impressive (Figure 4). There were

Figure 4—Clinical response at 2 weeks with Crest® Professional Whitestrips.

Table 3—Treatment Comparisons

Group	Adjusted Mean Change From Baseline (SE)	Treatment Difference (SE)	*P*-value
Δb* (yellow-blue)			
Strip (n = 10)	–2.16 (0.281)	–1.46 (0.325)	0.002
Tray (n = 10)	–0.70 (0.281)		
ΔL* (brightness)			
Strip (n = 10)	3.67 (0.388)	1.41 (0.452)	0.022
Tray (n = 10)	2.27 (0.388)		
ΔE* (composite color)			
Strip (n = 10)	4.55 (0.385)	2.00 (0.452)	0.003
Tray (n = 10)	2.55 (0.385)		

SE = standard error

no differences with respect to starting color scores, use, or other treatment factors that obviously contributed to this favorable response. In addition, two subjects in the tray group had no meaningful clinical response with respect to Δb*, the primary color parameter of interest in vital bleaching. Both of these subjects, a 30-year-old woman and a 59-year-old man, used tobacco products daily. While they had no meaningful reduction in yellow, both showed improvements in ΔL* of 1.63 and 3.97 units, respectively, which helps rule out noncompliance as a basis for the observed response. There were no reports of tooth sensitivity, gingival irritation, or other adverse events that may have contributed to low compliance by these subjects.

Trade publications describe at least 16 different suppliers of at-home, tray-based bleaching systems. To date, few of these formulations have been tested in adequate and well-controlled clinical trials and reported in peer-reviewed literature.

There were significant between-group differences with respect to the whitening benefit after 14 days of treatment. After adjusting for baseline, the strip group exhibited statistically significant improvements in tooth color for all parameters compared to the tray system (Table 3). For brightness (ΔL*) and overall color change (ΔE*), this represented a 62% to 78% gain in whitening for the strip system relative to the tray system. With respect to reduction in yellow, this 14-day adjusted mean Δb* was –2.16 and –0.70 units for the strip and tray groups, respectively, which represented a threefold decrease in yellow with the strip system compared with the color change seen after use of the tray system. Similar results were achieved without the high responder in the strip group. Despite the shorter treatment time (14 hours vs 28 hours), treatments differed statistically with respect to all of the measured color parameters, including Δa*, always favoring the strip group.

Tooth sensitivity and gingival irritation were the most commonly reported events (Table 4). These events were infrequent in number and generally "mild" in terms of subject-described severity. In addition to tooth sensitivity and gingival irritation, one subject in the strip group reported "mild" irritation on the tip of the tongue during strip treatment. None of these events were reported to lead to changes in the treatment regimen. There were

Table 4—Reported Tooth Sensitivity and Gingival Irritation by Severity

Parameter	Strip Group (n = 10)	Tray Group (n = 10)	Overall (n = 20)
Tooth Sensitivity			
Total: n (%)	2 (20%)	1 (10%)	3 (15%)
Mild severity: n	1	0	1
Moderate severity: n	1	1	2
Gingival Irritation			
Total: n (%)	3 (30%)	0 (0%)	3 (15%)
Mild severity: n	2	0	2
Moderate severity: n	1	0	1

no serious or severe adverse events and none of the subjects withdrew during the 14-day treatment period because of an adverse event.

Discussion

While both bleaching systems were effective in whitening teeth over a 14-day period, clinical response after using the strips was superior to the tray system despite the shorter contact times with the whitening strip. The whitening strip resulted in a 62% to 209% greater objective color change compared with the tray system. This superior response for the strip system was seen across all color parameters measured in this trial. For the important perceptual variable of yellow, the strip group experienced a 1.54-unit improvement over the tray group. How meaningful is this difference between the systems? In previous research, a different 20% carbamide peroxide tray-based bleaching system was reported to yield a 1.1-unit improvement relative to its 10% control.[8] Of note, this superiority was seen broadly across the patient population. With respect to the primary color variable of interest in this trial (Δb*), 90% of the subjects in the tray group had an observed response that was below that of the worst response in the strip group.

Besides the devices (strip or tray), there were several key differences between the systems studied in this trial, including contact time (14 hours or 28 hours), concentration (6.5% hydrogen peroxide or 10% carbamide peroxide equivalent), and gel dose (200 mg or 500 mg per treatment). Product differences in the manufacturer's packaging and usage instructions, esthetics, and other factors may have contributed to ease of use and overall compliance. With respect to the end user—the patient—the strip system was superior for whitening compared with the tray system. We speculate that a combination of the above factors likely contributed to the results seen in this trial.

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The digital imaging system in this study has been used in a number of other bleaching clinical trials. We prefer this method, especially for partially blinded research, because it yields an objective outcome over the entire facial surface of the anterior teeth. For the primary color parameter (Δb*), the clinical response with the 6.5% hydrogen peroxide strip system in this trial was remarkably consistent with previous research that used this method to study color in adults after bleaching. In this new study, we observed a 14-day Δb* for the Crest® Professional Whitestrips system of –2.16 units. In a separate clinical trial, 14-day use of the Crest® Professional Whitestrips system was reported to yield an

adjusted mean Δb* of –2.05 to –2.15, depending on the brushing regimen.[10] Adjusting for the higher peroxide concentration in these new strips, results are further consistent with outcomes reported from multiple clinical trials for the lower-concentration strip system.[11] This cross-study consistency, uncommon in comparative oral care clinical trials, validates the response observed in this trial. Although the authors have considerable clinical trial experience with respect to other bleaching systems, this represented our first objective evaluation of the Nite White® Excel 2 tray system. Despite following marketed instructions, the tray system in this trial yielded a relatively modest response relative to the strips and our previous research of other tray systems.[8] The limited bleaching effectiveness of the tray system in this trial cannot be discounted, given the otherwise consistent strip response seen compared to numerous other studies. Of course, causality cannot be determined from a trial of this type. Further research would be indicated to ascertain whether compliance with the 2-hour regimen or other factors contributed to the poor tray response in this trial.

Both systems were well tolerated. Only three subjects reported tooth sensitivity during the treatment period, two in the strip group and one in the tray group. In addition, 30% of the subjects in the strip group experienced minor gingival irritation sometime during the 14-day treatment period. This rate is consistent with that previously reported for the lower-concentration strip system. Also, system events were generally "mild" in severity and did not contribute to dropout.

To ensure blinding, we reported outcomes only during a 14-day head-to-head test. Over this period, the Crest® Professional Whitestrips tooth-whitening system was superior to Nite White® Excel 2 with respect to whitening. Extended use of this 6.5% hydrogen peroxide bleaching system should yield even greater efficacy.

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