Tooth-whitening efficacy of custom tray-delivered 9% hydrogen peroxide and 20% carbamide peroxide during daytime use: A 14-day clinical trial

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Objective: The purpose of this 14-day parallel, double blind clinical trial was to evaluate the tooth whitening efficacy of a 9% hydrogen peroxide gel (Colgate Visible White) relative to a 20% carbamide peroxide gel (Opalescence) positive control.

Methods: Forty-six consenting adults were randomly assigned to use one of the two products. All participants had 6 unrestored maxillary anterior teeth averaging a shade ranking score of 9 (A3) in the Vitapan Classical Shade Guide scale of 1 through 16 (lightest to darkest). Tooth whitening consisted of at-home 30-minute daily self-applications of the assigned product after brushing with a non-bleaching dentifrice. One of two calibrated examiners performed the baseline, 5-day, 7-day, and 14-day tooth shade evaluations for a given participant, utilizing the same Vita guide under unmodified color-corrected lighting conditions. Thirty-seven participants made all visits. Bleaching efficacy

was measured with respect to mean shift (reduction from baseline) in rank scores of the maxillary anterior teeth, in which baseline rank scores functioned as covariables.

Results: Both treatment groups exhibited statistically significant mean shade rank score improvements from baseline after 5,7, and 14 days at 3.14, 3.70 and 4.68 for Colgate Visible White and 1.60, 2.52 and 3.85 for Opalescence.

Conclusions: Between-group comparison shows that while Colgate Visible White (9% hydrogen peroxide) provides a statistically significant tooth whitening improvement over Opalescence (20% carbamide peroxide) after 5 days of self-application, both products have a similar whitening effect after 7 and 14 days.

Key words: Randomized Clinical Trial, Vital Tooth Bleaching, Dentistry.

he demand for esthetic dentistry has grown tremendously over the last decade as people seek to improve their smile. Patients want easy to use tooth whitening systems with fast results. The first publication describing at-home vital tooth whitening technique, (the so-called nightguard vital bleaching) (1) was partly responsible for such esthetic revolution. Dentistry has responded to these new patient demands with modifications to vital tooth whitening approaches: the use of different whitening agents; different concentrations of whitening agents; different frequencies of application; different product format; different application modes (2).

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Vital tooth whitening techniques can be classified into in-office, dentist prescribed at-home treatment, products purchased over-the-counter (OTC), or a combination of these. The most popular dentist-administered technique clearly has been nightguard vital bleaching. This approach has traditionally used a relatively low concentration of whitening agent delivered in a custom fabricated tray that is loaded by the patient and worn overnight. In-office vital bleaching, by contrast, generally involves the use of 25-35% hydrogen peroxide and requires short treatment times. In a randomized examiner blind study, Auschill, et al. (3) reported that although OTC, in-office and at-home vital bleaching were all effective removing extrinsic staining, at-home bleaching was significantly more accepted by patients compared to the in-office method. Because it is rare for in-office treatment to achieve desired tooth whitening after a single intervention, patients preferred the reduced chair-time of at-home tooth bleaching.

The original nightguard vital bleaching technique¹ involved the application of 10% carbamide peroxide (3.5% hydrogen peroxide) in a custom-fitted (0.02-inch) plastic guard to be worn 6 to 8 hours at night and achieved satisfactory tooth whitening in 2 to 6 weeks. There is little disagreement concerning the short-term effects of vital bleaching technique when conducted as originally described. Multiple case reports and small clinical studies have confirmed that the overnight use of 10% carbamide peroxide gel used in a bleaching tray produces predictable tooth whitening (4-11). According to a meta-analysis conducted by Niederman, et al. (12) 93 percent of the patients who bleached their teeth following the original technique, exhibited a change of two shade guide units greater than patients who received a placebo treatment and 20 percent of the patients achieved an improvement of five shade guide units.

At present, the original technique of nightguard vital bleaching has been modified as investigators seek to improve the efficacy of tooth whitening procedures. Some of the modifications to the technique include: the use of a softer custom-fitted guard; different concentrations of hydrogen peroxide or carbamide peroxide; one or more active bleaching intervals during daytime. The bulk of the research findings in recent published literature suggest that, as consequence of these modifications and the development of novel tooth whitening techniques, the concentration of the bleaching agent and the duration of the exposure time (active bleaching session) have emerged as the two most important factors in the efficacy of any bleaching treatment. Given similar modes of bleaching agent delivery, clinical trials have shown that an increase in the concentration of the bleaching agent promotes faster tooth color lightening from increased diffusion of hydrogen peroxide (13-16).

The modification of the traditional night guard vital bleaching technique to incorporate the use of bleaching agents at increased concentrations has lead to reports of increased tooth sensitivity (13-14,17). In order to minimize tooth sensitivity, tooth whitening protocols should consider prescribing shorter application times when using bleaching agents of higher concentrations (18). Because in vivo studies have shown that more than 50 percent of active whitening agent can remain in the bleaching tray after two hours of bleaching, (19-20). shortened active application times during daytime as opposed to the traditional overnight bleaching may be indicated when high concentrations of bleaching agents are used in order to avoid the potential for an increased incidence of tooth sensitivity.

A tooth whitening treatment option consisting of custom tray-delivered high concentration of bleaching agent and short active bleaching times through unextended lengths of treatment may result in a tooth whitening option that satisfies patients' demands for fast color shade improvement. Some manufacturers claim that a hydrogen peroxide bleaching agent under these circumstances should bring about faster results than a carbamide peroxide formulation of similar concentration. The claim is based on the fact that during short active bleaching sessions, unlike a hydrogen peroxide bleaching agent, a carbamide peroxide bleaching agent is unable to provoke immediate bleaching activity as it first needs to break down into hydrogen peroxide and urea upon exposure to a moist environment.

The purpose of this 14-day clinical trial was to evaluate the tooth whitening efficacy of a 9% hydrogen peroxide gel relative to a popular 20% carbamide peroxide gel positive control, utilizing the at-home tray-delivery procedure and daily thirty-minute applications.

Methods

This study was a phase III, randomized, single-center, parallel group, double blind clinical trial designed to evaluate tooth whitening efficacy of Colgate Visible White containing 9% hydrogen peroxide (9%HP) compared to Opalescence containing 20% carbamide peroxide (20%CP). The study received approval from the Medical Sciences Campus Institutional Review Board at the University of Puerto Rico. Alginate impressions for custom tray fabrication were made for all volunteers that fit the inclusion criteria and signed the written portion of the informed consent process. Participant selection criteria consisted of:

Inclusion Criteria

- 1. Healthy male and female subjects aged 21-68 years, inclusive.
- 2. Availability for the two weeks duration of the study.
- 3. Minimum average Vita Shade of A3 for all six maxillary anterior teeth.
- 4. Six natural maxillary anterior teeth must be present and free of or large restorations or extrinsic stains covering more than 1/3rd of the facial tooth surface or a maximum of one dental prosthetic crown/facial veneer.

Exclusion Criteria

- 1. The presence of orthodontic appliances.
- 2. The presence of tumors or significant pathology of the soft or hard tissues of the oral cavity.
- 3. The presence of moderate or advanced periodontal disease (ADA III or IV).

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- 4. The presence of five or more carious lesions requiring immediate care.
- The use of stain-inducing medications or oral use products one month prior to, or anytime during, the two weeks of the study.
- 6. Participation in any other clinical study or test panel in the last month.
- 7. Pregnant or lactating women.
- 8. Allergies to tooth whitening products, personal care consumer products, or their ingredients.

A total of 46 participants met the inclusion criteria and enrolled in the study; 28 females and 18 males, aged 25 to 64.

Custom tooth whitening trays were fabricated using 0.035-inch thick Soft-Tray material (Ultradent Products). Trays were made following the vacuum-formed technique and a scalloped design extending 2mm over the gingival tissues. Reservoirs (LC Block-Out Resin, Ultradent Products) restricted to 1mm short of the gingival margin and the proximal line angles of the maxillary anterior teeth and premolars were created for dispensing of the tooth whitening product. At baseline evaluations, the trays were placed and adjusted as needed to insure no impingement on the soft tissues or abrasion of the oral mucosa.

During all visit examinations, participants were asked about the presence of tooth or gingival sensitivity. In addition, all hard and soft tissues of the oral cavity were visually inspected by the examiner for the presence of adverse reactions.

Participants were assigned following a random list to one of the two treatment groups:

Group I: Colgate Visible White containing 9% hydrogen peroxide (9% HP).

Group II: Opalescence containing 20% carbamide peroxide (20%CP)

All participants were provided with their assigned product, a soft-bristled adult toothbrush and a non-whitening dentifrice (Colgate Great Regular Flavor). With the help of models and color pictures, all participants were given demonstrations and asked to (for each application):

Step 1: Thoroughly brush their teeth.

Step 2: Syringe just enough gel to fill the built-in reservoirs in the trays.

Step 3: Place filled mouth tray firmly in place over teeth.

Step 4: Wipe off any excess whitening gel with finger

Step 4: Wipe off any excess whitening gel with finger or toothbrush

Step 5: Wear filled mouth tray for 30 minutes daily.

Step 6: Remove the tray and brush their teeth with a wet toothbrush to remove any adhered whitening gel. Step 7: Rinse mouth tray under water, using a wet toothbrush to clean excess whitening gel from tray.

In order to further assure subject compliance with product use, participants received periodic phone calls to answer questions about the use of the assigned product and to remind them to return empty product-dispensing syringes at the next study visit.

The tooth shade examinations were performed and recorded at baseline and repeated after 5, 7 and 14 days of product use.

Participants were assigned to one of two examiners for the conduct of all tooth shade assessments under unchanged clinical conditions. To reduce variation between study visits, all shade examinations were performed in a single, neutral-colored windowless clinical operatory under color-corrected lighting. Tooth shade was measured on teeth number 6,7,8,9,10 and 11 using a Vitapan Classical Shade Guide scale of 1 through 16 (ranked lightest to darkest) as established by H. Rauter GmbJ & Co; Bad Säckingen, Germany. The shade guide tabs were arranged B1 to C4 representing the 1 to 16 scale as suggested by the manufacturer.

Shade rank scores (SRS) were determined for each participant for each examination by taking the means across the teeth scored. Shade changes between the baseline and each follow-up examination were quantified by calculating the difference in SRS. Comparisons among the study treatment groups were based upon an analysis of these mean scores.

Analysis of covariance (ANCOVA) was employed to compare the treatment groups with respect to mean shift (from baseline) in rank scores, in which the baseline rank scores was employed as a covariable. Post-ANCOVA pairwise comparison of the study groups was performed using paired t-tests. Comparisons within the treatment groups with respect to baseline shade rank were performed using analysis of variance. A level of significance of p = 0.05 was employed in all tests of hypothesis.

The examiners were calibrated previous to the conduct of the study until a kappa statistic value superior of 0.80 for inter and intra examiner reliability was reached. A gold standard examiner was available for consultation throughout the study.

Results

A total of 46 participants were randomly assigned to use one of the two products; one participant from each product group terminated participation in the study due to minor gingival discomfort and 7 other failed to keep at least one of the study visits for reasons unrelated to product use. Thirty seven participants, 23 of which were females (62%), composed the study population that completed all study visits (Table 1).

The mean Vita shade baseline rank scores observed for the participants who completed the study were 11.07 for

Table 1. Summary of Age and Gender Characteristics for Participants who Completed the Two-Week Clinical Study.

Treatment	Nun	ber of Par	Age		
	Male	Female	Total	Mean	Range
Opalescence (20% CP) ¹ Colgate Visible	8	8	16	44.00	25-59
White (9% HP) ²	6	15	21	46.33	25-64

- 1. Opalescence containing 20% carbamide peroxide
- 2. Colgate Visible White containing 9% hydrogen peroxide

the Colgate Visible White (9% HP) group and 10.82 for the Opalescence (20% CP) group. No statistically significant difference was indicated among these baseline observations (p>0.05) (Table 2).

The 9%HP group presented tooth color lightening improvements from baseline of 3.14, 3.70, and 4.68

Table 2. Summary of the Baseline Vita Shade Guide Rank Scores for Participants who Completed the Two-Week Clinical Study.

Treatment	n	Baseline Shade Rank Scores ¹	Significance ²	
Opalescence Colgate Visible White	16 21	10.82 ± 1.85 11.07 ± 2.01	p>0.05	

- 1. Baseline Vita Shade Rank Scores, Mean values \pm Standard Error.
- 2. Comparison of baseline means.

Table 3. Summary of 5, 7 and 14-Day Vita Shade Guide Rank Scores for Participants who Completed the Two-Week Clinical Study.

Days of Product Use	Product Group ¹	N	Shade Rank Scores ² (SRS)	Within-Treatment Analysis		Between-Treatment Analysis	
				SRS Reduction ³	Sig.4	Difference ⁵	Sig.6
5	20% CP 9% HP	16 21	9.22 ± 2.47 7.92 ± 2.86	1.60 ± 1.78 3.14 ± 1.75	p<0.05 p<0.05	1.54 ± 0.58	P<0.05
7	20% CP 9% HP	16 21	8.30 ± 2.16 7.37 ± 2.77	2.52 ± 2.13 3.70 ± 1.49	p<0.05 p<0.05	1.18 ± 0.60	p>0.05
14	20% CP 9% HP	16 21	6.97 ± 2.67 6.39 ± 2.69	3.85 ± 2.13 4.68 ± 1.58		0.83 ± 0.61	p>0.05

- 1. 9%HP = Colgate Visible White; 9%HP = Opalescence
- 2. Vita Shade Rank Scores after 3, 5, 7 and 14 days of product use, Mean values \pm Standard Error.
- 3. Reduction in shade rank scores (improvement) relative to baseline, Mean values ± Standard Error.
- 4. Significance of 3, 5, 7 and 14-day shade rank score improvements relative to baseline.
- 5. Between-group difference in shade rank score improvements, (9%HP-20%CP) \pm Standard Error
- 6. Significance of greater shade rank score improvement of 9%HP over 20%CP.

respectively after 5,7 and 14 days of product use. The shade rank score improvements from baseline produced by the use of the 20% CP product after 5,7 and 14 days of product use were 1.60, 2.52 and 3.85 (Table 3). All reported mean change improvements from their respective baseline shade rank scores were statistically significant (p<0.05).

Between-group comparison showed that, relative to the 20%CP group, the 9%HP group showed a statistically significant 1.54 greater shade rank score unit reduction in mean tooth shade rank score after 5 days of product use. The estimated 1.18 and 0.83 greater shade rank score unit reductions for the 9%HP formulation over the 20%CP formulation respectively after 7 and 14 days of product use, were not statistically significant calculations(p>0.05) (Table 3).

Discussion

This study was designed to evaluate the *in vivo* tooth whitening efficacy of Colgate Visible White containing 9% hydrogen peroxide (9% HP) relative to Opalescence containing 20% carbamide peroxide (20% CP), which breaks down into an active bleaching agent concentration of approximately 7.2% hydrogen peroxide. Both products were tested under similar clinical conditions, tray-delivered at-home daily 30-minute product applications for 14 days.

Both the 9% HP and 20% CP tooth whitening products were effective when used once daily for 30-minute applications for 5, 7 and 14 days. The 9% HP formulation showed greater tooth whitening efficacy than the 20% CP

formulation after 5 days of product use. Similar tooth whitening efficacy was observed for both products after 7 and 14 days of product application.

It is difficult to compare the results of this study with the results of published investigations because of significant variations in study design, in vivo vs in vitro, concentration of active agents, full length of treatment, or mode of daily product application. A recent review of the literature by Joiner² observed that, in general, the efficacy of HP containing products are approximately the same when compared with CP containing products with equivalent or similar HP content and delivered using similar format

and formulations, either tested in vitro or in vivo.

Few studies have compared tooth whitening products with relatively high concentrations of CP and HP at what would be similar hydrogen peroxide concentration once CP breaks down into its active tooth whitening agent form. Mokhlis et al.²¹ compared the use of tray-delivered 7.5% HP and 20%CP (7.2% hydrogen peroxide) one hour applications twice a day for two weeks in a double-blind clinical study. Colorimeter data showed a significantly lighter tooth whitening effect of 20%CP during the two weeks of active treatment, but no significant differences in tooth color lightness when evaluated 10 weeks later. The authors speculated that the two one-hour active bleaching sessions per day had a strong effect in favor of the tooth whitening efficacy of the 20%CP product over the 7.5% HP product. The argument was based on the fact that since CP needs to first break down to produce hydrogen peroxide, given relatively long active bleaching time sessions, active hydrogen peroxide derived from the 20% CP can remain in contact with the enamel surface past the degradation time of all or most of the active bleaching activity of 7.5% HP. It could be argued that relatively short tooth whitening sessions of 30 minutes per day, as employed in the present study, could favor the bleaching efficacy of the HP product over the CP product because less net degradation of hydrogen peroxide from the HP product is expected through a shorter bleaching session and because the active hydrogen peroxide from the HP product should be readily available to the tooth surfaces it is meant to bleach, while the CP formulation is unable to provoke immediate bleaching activity as it first needs to break down into hydrogen peroxide and urea.

The presence of a greater concentration of active hydrogen peroxide from the 9%HP versus the resultant 7.2% hydrogen peroxide from the 20%CP formulation during the active bleaching sessions should have been expected to further favor an increased tooth whitening efficacy of Colgate Visible White (9%HP) over Opalescence (20%CP). The results support the findings of *in vitro* (13,22) and *in vivo* (16-18) studies regarding the efficiency in tooth whitening with increased tooth whitening agent concentrations. All of the cited studies also concluded that, given greater length of time (greater number of active bleaching sessions) for product use, the lower concentration products will achieve the same results as higher concentrations.

The whitening systems tested produced little tooth sensitivity or gingival irritation. Given the use of higher concentrations of whitening agents, the active bleaching sessions were reduced in time length and frequency of daily applications, in order to avoid a large incidence of tooth sensitivity and gingival irritations. Some participants reported mild sensitivity during the study but, in most cases disappeared before the end of the active bleaching sessions. Two participants, one from each study group, experienced mild gingival irritations towards the interproximal-palatal gingival margins of the whitened maxillary anterior teeth after 3 days of active bleaching. The examiners noted that all irritations occurred between teeth that shared no interproximal contact. The authors speculate that despite the mesio-distal limitations of the built-in reservoirs in the custom trays, in the absence of anterior interproximal tooth contact, excess of active bleaching agent may have spilled toward affected areas where participants were unable to wipe it off. Both participants decided to terminate their participation in the study.

Conclusions

Within the limitations of the study, the following conclusions can be drawn:

Both 9% hydrogen peroxide and 20% carbamide peroxide products effectively whitened teeth after 5, 7 and 14 days of once-a day thirty-minute applications.

Colgate Visible White (9% hydrogen peroxide) produced a statistically significant tooth shade improvement compared to the tooth whitening effect of Opalescence (20% carbamide peroxide) after 5 days of product use.

Colgate Visible White (9% hydrogen peroxide) and Opalescence (20% carbamide peroxide) had a similar whitening effect after 7 and 14 days of use.

Both tooth whitening products tested produced little tooth sensitivity or gingival irritation.

Resumen

Objetivo: El propósito de este estudio clínico paralelo doblemente ciego de 14 días fue evaluar la eficacia en el blanqueamiento de los dientes de una gelatina de peróxido de hidrógeno al 9% (Colgate Visible White) en relación con el control positivo de gelatina de peróxido de carbamida (Opalescence). Métodos: Cuarenta y seis adultos consintieron y fueron asignados aleatoriamente a uno de dos productos. Los participantes tenían 6 dientes anteriores maxilares no restaurados y en promedio tenían una puntuación de color de 9 (A3) en la guía de color Vitapan Classical cuya escala es de 1 al 16 (más claro al más oscuro). El blanqueamiento de dientes consistió en auto-aplicaciones del producto asignado en sus hogares diariamente por 30 minutos luego de cepillarse con una pasta dental no-blanqueadora. Uno de dos examinadores calibrados evaluaron el color de los dientes para cada participante en la visita inicial, 5 días, 7 días y 14 días utilizando la misma guía de color Vita bajo condiciones de iluminación no corregidas para color. Treinta y siete participantes completaron todas las visitas. La eficacia del blanqueamiento se midió con respecto al cambio promedio en rango de puntuación del color de los dientes anteriores maxilares, en los cuales el rango de puntuaciones funcionó como covariables. **Resultados:** Ambos tratamientos exhibieron mejoras estadísticamente significativas en los rangos promedios de puntuaciones de color de la visita inicial a 5,7 y 14 días de 3.14, 3.70 y 4.68 para Colgate Visible White y 1.60, 2.52 y 3.85 para Opalescente. **Conclusiones:** La comparación entregrupos demuestra que mientras Colgate Visible White (peróxido de hidrógeno al 9%) provee una mejora en el blanqueamiento de los dientes estadísticamente significativa sobre Opalescence (peróxido del carbamide al 20%), después de 5 días de la auto-aplicación, ambos productos tienen un efecto en el blanqueamiento de los dientes similar después de 7 y 14 días.

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