©Operative Dentistry, 2018, **43-3,** 272-281

Double-blind Randomized Study to Evaluate the Safety and Efficacy of Over-the-counter Tooth-whitening Agents Containing 2.9% Hydrogen Peroxide

YM Kim • AN Ha • JW Kim • SJ Kim

Clinical Relevance

This study supports the safety and efficacy of over-the-counter tooth-whitening products containing 2.9% hydrogen peroxide.

ABSTRACT

Objectives: In this double-blind randomized study, we evaluated the safety and efficacy of over-the-counter (OTC) bleaching products that included 2.9% hydrogen peroxide (H_2O_2) with two methods of application: strip and paint-on.

Methods and Materials: A commonly used product was selected for each type (strip and paint-on) of OTC bleaching agent. In total, 75 volunteers were assigned randomly into five groups: two test groups (strip and paint-on), two negative control groups (products without H_2O_2), and one positive control group (dentist-supervised home bleaching). The tooth shade was evaluated with a spectrophotometer and Vita shade guide at baseline and 2 weeks and 4 weeks after use. To document any adverse reactions, such as hypersensitivity or tissue irritation, all patients were examined and the Gingival Index (GI), Plaque Index (PI), and a visual analog scale (VAS) measuring the cold response were obtained.

Results: There were significant differences among the five groups ($p<0.001$). The positive control showed the greatest color changes; then, in decreasing order, the strip-type test group, paint-on-type test group, and negative controls. The strip-type bleaching agent was significantly more effective than the paint-on-type agent and the negative control, while it

Yemi Kim, DDS, MSD, PhD, assistant professor, Department of Conservative Dentistry, College of Medicine, Ewha Womans University, Seoul, Korea

Aena Ha, DDS, Department of Conservative Dentistry, College of Medicine, Ewha Womans University, Seoul, Korea

Jin-Woo Kim, DDS, MSD, PhD, assistant professor, Department of Oral & Maxillofacial Surgery, College of Medicine, Ewha Womans University, Seoul, Korea

*Sun-Jong Kim, DDS, MSD, PhD, professor, Department of Oral & Maxillofacial Surgery, College of Medicine, Ewha Womans University, Seoul, Korea

*Corresponding author: 1071, Anyangcheon-ro, Yangcheon-gu, Seoul, 07985 Republic of Korea; e-mail: oralsurgeonsj@gmail.com

DOI: 10.2341/16-379-C

was significantly less effective than the dentist-supervised home bleaching. Regardless of the treatment group, the canines showed greater color changes than did the central or lateral incisors. Some cases of gingival irritation and hypersensitivity were observed, but they were mild and reversible. GI, PI, and VAS scores were not significantly changed.

Conclusions: Within the limitations of this study, the results indicated that the strip-type and paint-on-type OTC bleaching agents were significantly less efficacious than was dentist-supervised home bleaching; however, they showed acceptable safety and efficacy. The strip-type was more effective than was the paint-on-type in this study.

INTRODUCTION

Because of increased demand for tooth bleaching and interest in dental esthetics, various bleaching products and methods have been introduced. Among such products is a dentist-supervised home bleaching system with a custom tray. The product was developed by Haywood and Heymann and offers an innovative approach to the field of tooth bleaching.[1] Since 2000, affordable and convenient over-the-counter (OTC) products have been manufactured for the comfort of consumers. OTC products are categorized based on the delivery method of the bleaching agent, and include prefabricated trays, whitening strips, and paint-on applications.[2] Products are also available as toothpaste, chewing gum, mouth rinse, and floss[3]; however, those products have lower efficacies compared with strips or paint-on products.[3]

Despite the increasing use of OTC at-home bleaching agents, they may not be as effective as dentist-supervised bleaching because of their low concentrations of hydrogen peroxide (H_2O_2).[2-6] Additionally, incorrect use of these OTC agents could lead to adverse effects.[2-6] In addition, there have been few well-organized clinical trials examining the efficacy and side effects of OTC bleaching products. This is particularly true for products containing less than 3% H_2O_2.[2,4,7-9] Thus, the present study was conducted to evaluate the efficacy and safety of some commonly used OTC bleaching products based on two methods of application (strip and paint-on), comparing them with negative controls that did not contain H_2O_2. The null hypothesis was that there are no differences in the effectiveness of different application methods.

METHODS AND MATERIALS

Commercially available tooth-whitening products were classified according to their application methods. A negative control containing the same ingredients as the selected product, except for H_2O_2, was manufactured, and for a positive control, a dentist-supervised home-bleaching product was used. In total, 75 subjects were recruited who participated in this randomized, double-blind, and placebo-controlled study.

Commercially Available Tooth-Whitening Products

Initially, the tooth-whitening products were categorized into strip, paint-on, and gel-tray products, and a common product was selected from each group. Claren White Now strips (LG Household and Health Care, Seoul, Korea), and White Now dental whitening pen gels (LG Household) were chosen as the strip and paint-on products, respectively. The same manufacturer also provided a test gel-tray product that included 2.9% H_2O_2. However, the gel-tray product was excluded from this study due to adverse effects during a preliminary study. Specifically, when the gel-type bleaching agent directly contacted the oral mucosa, it caused soreness.

The selected strip and paint-on products contained 2.9% H_2O_2. Negative controls containing the same ingredients as the product, except for the whitening agent H_2O_2, were used in the same way as the test groups. As a positive control, a dentist supervised home-bleaching product, the Opalescence tooth whitening gel (Ultradent Products Inc, South Jordan, UT, USA) was used; it contained 10% carbamide peroxide, which is equivalent to 3.62% H_2O_2. Treatments were performed twice daily for 30 minutes each, and continued for 4 weeks according to the manufacturer's directions and the results of previous studies.[8,10]

Selection of Participants

Volunteers over 19 years old interested in tooth bleaching were recruited to participate after obtaining approval from the institutional review board of the Ewha Womans University Hospital. Maxillary and mandibular anterior teeth of volunteers with good systemic and oral health and mild-to-moderate tooth discoloration, screened through oral examinations and questionnaires, were enrolled. Subjects with extensive resin, porcelain restorations, dental caries and wear, or hypersensitivity due to gingivitis or periodontitis were excluded (Table 1).

Table 1: *Criteria Used for Selection and Exclusion of Participants*

Inclusion Criteria	Exclusion Criteria
1. Good systemic and oral health	1. No informed consent
2. Moderate and relatively mild tooth discoloration	2. Insufficient teeth for bleaching
3. Informed consent from adults over 19 years of age	3. Resin or porcelain restoration in the anterior dentition
4. Understands the purpose of the experiment	4. Pulpal inflammation due to dental caries or wear
	5. Hypersensitivity due to gingivitis or periodontitis
	6. Excessive discoloration due to drugs or congenital developmental disorder

The experiment was designed to be carried out with seven groups (three test groups, three negative controls, and one positive control), but due to complications in a preliminary study, the gel tray–type product was removed from the experiment. Thus, there were, in total, 75 participants, 15 in each of the five groups (two test groups, two negative controls, and one positive control). The recruited subjects were randomly assigned to groups through a code provided by SAS software. Of the 75 participants, 64 were female, and the overall average age was 30.3 years (±5.95 years).

Application and Analysis of Tooth-Bleaching Agent

During the first visit, informed consent was obtained after an explanation of the study, and the corresponding tooth-bleaching agent was provided once the subject was assigned randomly to a group. To ensure blinding of the research team, products were sealed in identical opaque containers, and numbered by an independent researcher. Thus, neither the investigators nor the participants knew which treatment was administered. Both verbal and written tooth-bleaching agent application instructions and precautions were given, and the participants were told to call immediately in case of an adverse reaction. In total, three visits, including the first, were scheduled, and tooth shade improvement and adverse reactions were evaluated.

Visit 1 (Screening and Baseline)—After an explanation and discussion of the experiment, the volunteers were screened using the selection and exclusion criteria. Written consent, demographic information, and patient histories were collected from the subjects. Baseline measures were assessed, and the tooth-bleaching agents were provided after random assignment to a group. Each participant received an identifying number as well as a numbered product in a sealed, opaque container. Written instructions were also provided detailing the storage and application protocols. Participants were instructed to avoid food and drinks that might stain teeth, including tea, coffee, red wine, and red fruits. To standardize oral hygiene, participants received soft-bristled, adult toothbrushes and toothpastes that lacked whitening agents. Participants were instructed to brush their teeth three times daily for at least 3 minutes each time for 4 weeks. A researcher not involved in collecting tooth-color measurements administered the tooth-bleaching products to each patient. Tooth-color measurements were taken by one evaluator using a spectrophotometer, and two or three others using a Vita shade guide. The evaluators who measured tooth color did not know to which group each patient belonged.

Visit 2 (2 Weeks)—After using the bleaching agent for 2 weeks, an effectiveness evaluation was performed. To document any adverse reactions, such as hypersensitivity or tissue irritation, all patients were examined through an ocular inspection, detailed questions, hypersensitivity test, and photographic record.

Visit 3 (4 Weeks)—After using the bleaching agent for 4 weeks, an effectiveness evaluation was performed, and adverse reactions were documented in the same way as for visit 2.

Evaluation of Clinical Efficacy

A spectrophotometer, accepted as the gold standard for verifying the effectiveness of bleaching agents, and a Vita shade guide, the most commonly used shade guide in the clinic, were used to measure changes in tooth shade. All examinations were performed at the same location using the same light source while participants assumed the same position.

CIE Lab* Spectrophotometer Measurements

After calibration of the spectrophotometer (SpectroShade Micro, Verona, Italy), the head of the instrument was placed near and perpendicular to the middle third of the labial surface of the anterior tooth to assess its shade. CIE Lab* was selected for color specification mode, and measurements were taken three times each and averaged to be used for that tooth's CIE Lab* value. To calculate the similar

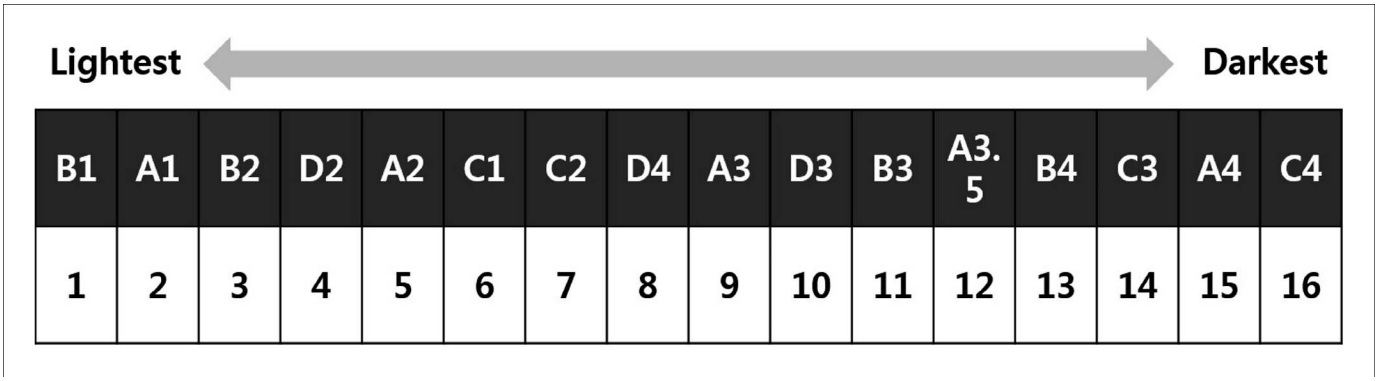

Figure 1. *Numeric scores of Vitapan Classical shade guide in decreasing order of brightness.*

ΔE, the measured L*, a*, b* values were entered in the equation below.

$$\Delta E^* = ((L_2 - L_1)^2 + (a_2 - a_1)^2 + (b_2 - b_1)^2)^{1/2}$$

where ΔE is the shade difference; L_1, a_1, and b_1 are the CIE Lab* values before bleaching; and L_2, a_2, and b_2 are the CIE Lab* values after bleaching. The lightness (L) value represents brightness, ranging from 0 to 100, and the number directly increases with the brightness. A* and b* values indicate chroma (+a* [red], −a* [green], +b* [orange], −b* (blue]), ranging from −60 to +80, and the larger the absolute value, the more saturated the color.

Vita shade

According to the traditional method of selecting the shade most closely matching the tooth, hue (designated as A, B, C, D) was chosen followed by the chroma (designated as numbers 1 through 4). The tooth shade can be classified into 16 steps, and each step was given a numerical score, which was used to calculate the difference in the numbers before and after bleaching (Figure 1). The shades were chosen using the same method for the 12 maxillary and mandibular anterior teeth. Two independent researchers determined the shade at the same time and location. When there was a disagreement, a more experienced third examiner participated in the decision. Prior to examination, all investigators were calibrated using the Vita shade guides (Vitapan Classical shade guide, Vita Zahnfabrik, Bad Säckingen, Germany) and using the sample of 10 patients with characteristics similar to those of the study subjects. All investigators correctly assigned shades in at least 85% of cases.

Safety Assessment

During the first visit, the Gingival Index (GI), Plaque Index (PI), and a visual analog scale (VAS) measuring the cold response were obtained, and these values continued to be recorded in the follow-up visits to evaluate the safety of the tooth whitening agents.

Gingival Index (GI) by Löe and Silness—Score Criteria: 0, no inflammation; 1, mild gingival inflammation and change in color, slight edema, no bleeding on probing; 2, moderate inflammation and glazing, erythema, bleeding on probing; 3, severe inflammation, erythema and hypertrophy, ulceration, spontaneous bleeding tendency.

Plaque Index (PI) by Löe and Silness—Score Criteria: 0, absence of plaque; 1, film of plaque present on the free gingival margin and adjacent area of the tooth. Plaque observed only after using disclosing solution or a probe on the tooth surface; 2, moderate accumulation of plaque in the gingival pocket, margin, and surrounding tooth surface, observed with the naked eye; 3, abundance of plaque in the gingival pocket and margin.

Visual Analog Scale (VAS)—The intensity of discomfort felt by the patient was marked on a 100-mm horizontal line with the numbers 0 (no pain) and 10 (severe pain) at each end. All subjects marked a vertical line indicating the severity of hypersensitivity to cold, tested with an ice stick.

Statistical Analysis

Statistical analyses were performed using the SPSS software (ver. 21.0; SPSS, Inc, Chicago, IL, USA). Tooth color changes were analyzed using a linear mixed model, regardless of tooth location. Statistical analysis of color change for each tooth type was

Table 2: *Spectrophotometric Analysis After Bleaching for 2 Weeks*

Tooth Location		Group					
		DSHB[a]	Strip Type (Test)	Strip Type (-)[b]	Paint-On Type (Test)	Paint-On Type (-)	*P* Value
Upper	Central incisor	3.20 ± 1.32^{Ac}	2.61 ± 1.16^{AB}	0.93 ± 0.41^{C}	1.58 ± 0.85^{BD}	1.32 ± 0.98^{CD}	<0.001
	Lateral incisor	4.19 ± 1.96	2.82 ± 1.09^{A}	1.36 ± 0.58^{B}	1.59 ± 0.97^{AC}	1.21 ± 0.98^{BC}	<0.001
	Canine	6.21 ± 2.51	4.58 ± 1.66	1.70 ± 0.80^{A}	2.26 ± 1.42^{B}	1.50 ± 0.71^{AB}	<0.001
Lower	Central incisor	3.07 ± 1.47	1.87 ± 0.87^{AB}	1.13 ± 0.93^{AC}	1.64 ± 0.98^{BD}	0.99 ± 0.62^{CD}	<0.001
	Lateral incisor	3.92 ± 1.73	2.35 ± 1.02^{A}	0.95 ± 0.40^{B}	1.66 ± 1.04^{AC}	1.14 ± 0.51^{BC}	<0.001
	Canine	5.44 ± 2.35	3.47 ± 1.46	1.57 ± 0.77 ^{A}	1.88 ± 0.83^{B}	1.46 ± 0.71^{AB}	<0.001
Total		4.34 ± 1.71	2.95 ± 1.02	1.26 ± 0.46^{A}	1.77 ± 0.74^{B}	1.27 ± 1.54^{AB}	<0.001

[a] *DSHB indicates dentist-supervised home bleaching.*
[b] *(-) indicates negative control.*
[c] *Same letters indicate that the values are statistically similar for each row* ($p<0.05$).

analyzed using one-way analysis of variance with Tukey's multiple comparison test. All values were considered statistically significant when $p<0.05$.

RESULTS

Assessment of Shade Improvement

The baseline color parameters for each treatment group were not significantly different. After bleaching, spectrophotometric assessments revealed an increase in L and a decrease in chroma (a and b). Thus, decreased scores were observed using the Vita shade guide. The positive control showed the highest color changes in all tooth positions; then, in decreasing order, the strip-type test group, paint-on-type test group, and negative controls. The strip-type bleaching agent was significantly more effective than was the paint-on-type agent, while it was significantly less effective than the dentist-supervised home bleaching. Regardless of the treatment group, the canine groups showed greater color changes than did the central and lateral incisor groups in both upper and lower jaws (Tables 3-6).

Spectrophotometer

2 Weeks (Table 2 and Figure 2)—In all tooth locations, the positive control showed a significant difference vs the other treatment groups, except for the upper central incisor treated with the strip-type bleaching agent ($p=0.485$). When the strip-type and the paint-on-type were compared, only the canine groups were significantly different (upper: $p=0.01$, lower: $p=0.023$). When the test group was compared with the negative control, there was a significant difference except for the lower central incisor ($p=0.285$) in the strip-type. In contrast, the paint-on-type did not show a significant difference between the test and negative control groups ($p=0.456$).

4 Weeks (Table 3 and Figure 3)—In all tooth locations, the positive control showed a significant difference compared with the other treatment groups, except for the upper central incisor treated with the strip-type bleaching agent ($p=0.466$). Between the strip-type and paint-on-type, unlike the results at 2 weeks, there were significant differences except for the lower incisors (lower central incisor: $p=0.692$, lower lateral incisor:

Table 3: *Spectrophotometric Analysis After Bleaching for 4 Weeks*

Tooth Location		Group					
		DSHB[a]	Strip Type (Test)	Strip Type (-)[b]	Paint-On Type (Test)	Paint-On Type (-)	*P* Value
Upper	Central incisor	4.27 ± 1.36^{Ac}	3.55 ± 1.52^{A}	0.88 ± 0.25^{B}	1.95 ± 1.4^{C}	1.20 ± 0.22^{BC}	<0.001
	Lateral incisor	5.58 ± 1.97	4.11 ± 1.68	1.46 ± 0.79^{A}	1.94 ± 0.95^{B}	1.10 ± 0.79^{AB}	<0.001
	Canine	08.1 ± 2.77	6.16 ± 2.42	2.03 ± 0.79^{A}	2.53 ± 1.48^{B}	1.34 ± 0.81^{AB}	<0.001
Lower	Central incisor	4.02 ± 1.71	2.48 ± 0.29^{A}	1.07 ± 0.90^{B}	1.87 ± 1.51^{AC}	1.38 ± 0.23^{BC}	<0.001
	Lateral incisor	5.01 ± 1.90	3.30 ± 1.38^{A}	1.11 ± 0.47^{B}	2.19 ± 1.41^{AC}	1.44 ± 1.07^{BC}	<0.001
	Canine	7.11 ± 2.87	4.70 ± 2.13	1.70 ± 0.90^{A}	2.26 ± 1.13^{B}	1.50 ± 0.75^{AB}	<0.001
Total		5.68 ± 1.91	4.05 ± 1.48	1.36 ± 0.43^{A}	2.12 ± 1.09^{B}	1.32 ± 0.57^{AB}	<0.001

[a] *DSHB indicates dentist-supervised home bleaching.*
[b] *(-) indicates negative control.*
[c] *Same letters indicate that the values are statistically similar for each row* ($p<0.05$).

Table 4: *Color Changes Based on the Vita Shade Guide After Bleaching for 2 Weeks*

Tooth Location		Group					
		DSHB[a]	Strip Type (Test)	Strip Type (−)[b]	Paint-on Type (Test)	Paint-on Type (-)	*P* Value
Upper	Central incisor	−3.13 ± 1.51^{ABc}	−1.93 ± 1.83^{ACD}	−0.70 ± 1.62^{CDE}	−2.00 ± 1.04^{BD}	−0.23 ± 0.92^{E}	<0.001
	Lateral incisor	−3.43 ± 1.52^{AB}	−2.27 ± 1.83^{AC}	−0.50 ± 2.35^{D}	−2.11 ± 1.64^{BCE}	−0.50 ± 0.85^{DE}	<0.001
	Canine	−4.20 ± 1.95	−2.50 ± 1.72^{A}	−0.80 ± 1.98^{B}	−1.32 ± 1.41^{AC}	−0.17 ± 0.84^{BC}	<0.001
Lower	Central incisor	−2.97 ± 2.07	−0.53 ± 0.74^{AB}	−0.80 ± 1.86^{AC}	−0.42 ± 0.83^{BD}	0.00 ± 1.02^{CD}	<0.001
	Lateral incisor	−2.77 ± 2.17^{AB}	−1.80 ± 1.58^{ACD}	−0.73 ± 1.79^{CE}	−1.00 ± 1.63^{BDF}	−0.63 ± 1.20^{EF}	0.005
	Canine	−3.20 ± 2.11^{A}	−2.00 ± 2.15^{AB}	0.37 ± 2.23^{C}	−0.96 ± 1.60^{BD}	0.33 ± 1.17^{CD}	<0.001
Total		−3.28 ± 1.35^{A}	−1.84 ± 1.01^{AB}	−0.52 ± 1.39^{C}	−1.30 ± 0.87^{BD}	−0.25 ± 0.43^{CD}	<0.001

[a] *DSHB indicates dentist-supervised home bleaching.*
[b] *(-) indicates negative control.*
[c] *Same letters indicate that the values are statistically similar for each row* ($p<0.05$).

$p=0.173$). The strip-type bleaching agent was significantly brighter than the negative control at all tooth locations (lower central incisor: $p=0.027$, others: $p<0.001$), but the paint-on-type was not significantly different from the negative control for any tooth location using the bleaching agent for 2 weeks more ($p=0.408$).

Vita shade guide

2 Weeks (Table 4 and Figure 4)—The positive control was better than the strip-type only on the upper canines and lower central incisors (upper canine: $p=0.045$, lower central incisor: $p<0.001$). Also, compared with the paint-on-type, the positive control was more effective on the upper canines and lower central incisors and canines (upper canines and lower central incisors: $p<0.001$, lower canine: $p=0.019$). The strip-type and the paint-on-type were not significantly different ($p>0.309$). The strip-type was significantly different from the negative control on the upper lateral incisors and canines and the lower canines (upper lateral incisor: $p=0.046$, upper canine: $p=0.045$, lower canine: $p=0.009$). The paint-on-type was not significantly different, compared with the negative control, except for the upper central incisor ($p=0.012$).

4 Weeks (Table 5 and Figure 5)—For the upper central incisor, the positive control, strip-type, and paint-on-types were not significantly different (strip: $p=0.577$, paint-on: $p=0.147$). For lower lateral incisors and canines, the results after 2 weeks of using the bleaching agents showed that the positive control was more effective than the other two types, but after 4 weeks, the positive control and strip-type were not significantly different (lower lateral incisor: $p=0.144$, canine: $p=0.117$). The strip-type and the paint-on-type agents were not significantly different ($p>0.339$). The strip-type agent was significantly effective vs the negative control, but not for the lower incisors (central incisor: $p=0.997$, lateral incisor: $p=0.061$). The paint-on-type agent after 2 weeks was significantly effective only on the upper central incisors. However, after 4 weeks, this agent was significantly effective on all the upper anterior teeth, but not on the lower teeth (lower: $p>0.333$).

Table 5: *Color Changes Based on the Vita Shade Guide After Bleaching for 4 Weeks*

		Group					
		DSHB[a]	Strip Type (Test)	Strip Type (-)[b]	Paint-on Type (Test)	Paint-on Type (-)	*P* Value
Upper	Central incisor	−3.83 ± 1.89^{ABc}	−3.00 ± 1.85^{AC}	−0.53 ± 1.30^{D}	2.50 ± 1.61^{BC}	-0.63 ± 0.77^{D}	<0.001
	Lateral incisor	−5.63 ± 2.07	−2.53 ± 1.60^{A}	−0.50 ± 2.64^{B}	−3.25 ± 2.00^{A}	-1.00 ± 1.24^{B}	<0.001
	Canine	−7.13 ± 2.09	−4.57 ± 2.15^{A}	−1.03 ± 2.41^{B}	−3.14 ± 1.76^{A}	-4.00 ± 1.69^{B}	<0.001
Lower	Central incisor	−3.13 ± 2.13	−0.93 ± 1.22^{AB}	−0.73 ± 1.98^{AC}	−0.75 ± 1.28^{BD}	0.07 ± 1.28^{CD}	<0.001
	Lateral incisor	−3.70 ± 1.82 ^{A}	−2.27 ± 1.59^{ABC}	−0.60 ± 1.59^{BD}	−1.61 ± 1.91^{CE}	-0.73 ± 1.44^{DE}	<0.001
	Canine	−5.57 ± 2.71 ^{A}	−3.67 ± 2.14^{AB}	0.10 ± 1.93^{C}	−1.46 ± 2.34^{BD}	0.03 ± 1.29^{CD}	<0.001
Total		−4.83 ± 1.30	−2.83 ± 1.15^{A}	−0.54 ± 1.40^{B}	−2.12 ± 0.94^{A}	−0.44 ± 0.75^{B}	<0.001

[a] *DSHB indicates dentist-supervised home bleaching.*
[b] *(-) indicates negative control.*
[c] *Same letters indicate that the values are statistically similar for each row* ($p<0.05$).

Table 6: *Changes in VAS Test Values After Bleaching for 2 or 4 Weeks**

Change in VAS	Group				
	DSHB[a]	Strip Type (Test)	Strip Type (-)[b]	Paint-on Type (Test)	Paint-on Type (-)
2 wk	0.23 ± 6.34	−1.45 ± 15.81	3.79 ± 8.70	−1.18 ± 6.78	1.68 ± 5.79
4 wk	−3.43 ± 8.04	−1.03 ± 13.89	−0.52 ± 5.92	−4.09 ± 9.04	−0.39 ± 6.47

[a] *DSHB indicates dentist-supervised home bleaching.*
[b] *(-) indicates negative control.*
* *No statistically significant difference was found between groups or before and after tooth bleaching* ($p>0.05$).

Safety Assessment

Each patient in this study completed the Gingival Index (GI), Plaque Index (PI), and visual analog scale (VAS). All of them scored 0 or 1 on the GI and PI at the first visit. After using the bleaching agents, GI scores of all patients were unchanged, and PI scores on two patients changed. However, although these scores changed, they were not considered indicative of unfavorable conditions because the maximum score was 1, while most other scores were 0. No significant difference was observed in the VAS between groups or before or after bleaching ($p>0.05$; Table 6). Although no severe gingival irritation or hypersensitivity was reported, some mild and reversible cases of oral mucosal irritation and hypersensitivity were observed. Four patients using the paint-on-type test product and four patients using paint-on-type negative control product complained of mucosal irritation, especially on the lower lip mucosa. The symptoms subsided within a few minutes after rinsing out the agent.

DISCUSSION

Although the Vita shade guide is the most commonly used method of measuring changes in tooth color, visually discerning the shade is impacted by various factors, including the light source, color of the gingiva, makeup, angle of measurement, skill of the examiner, and eye fatigue.[11,12] Also, because the Vita shade guide has a limited range of colors, meaning that it cannot provide true CIE Lab* values and changes in shade cannot be accurately measured.[12,13] However, the spectrophotometer is considered the gold standard for evaluating the effectiveness of a tooth bleaching agent, due to its high reproducibility and objectivity.[14] Despite this, reflections on the tooth surface, diameter and direction of the spectrophotometer tip, and the background surrounding the tooth can affect shade matching,[15] so evaluators must be fully aware of spectrophotometer use. Thus, the error range should be minimized through appropriate use of the Vita shade guide and the spectrophotometer, accurate interpretation of results, and repeated measurements. In this study, both methods were used to evaluate changes in shade after bleaching.

These changes were examined using the ΔE value, which was calculated with the coordinates of L, a, and b. A change is considered to be imperceptible to the naked eye when the ΔE value is between 0 and 2, barely perceptible when between 2 and 3, generally perceptible between 3 and 8, and readily perceptible when the value is over 8.[16] Also, it has been suggested that a value below 3.3 is clinically

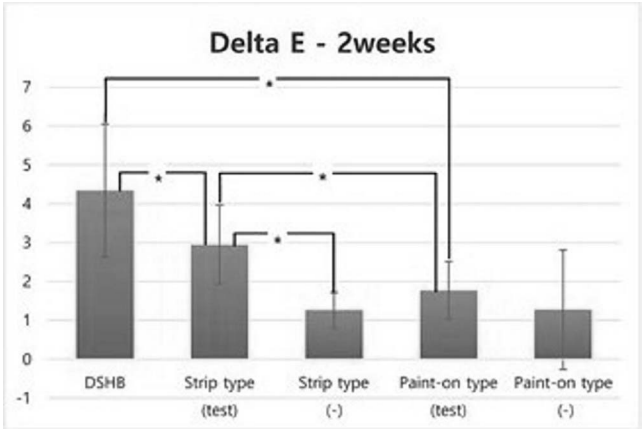

Figure 2. *Spectrophotometer: color changes after bleaching for 2 weeks.* *$p<0.05$.

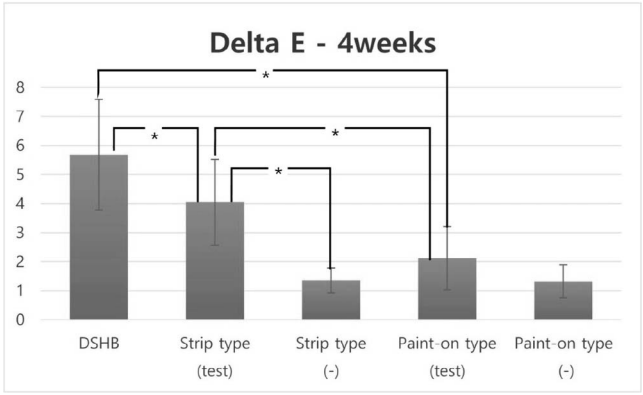

Figure 3. *Spectrophotometer: color changes after bleaching for 4 weeks.* *$p<0.05$.

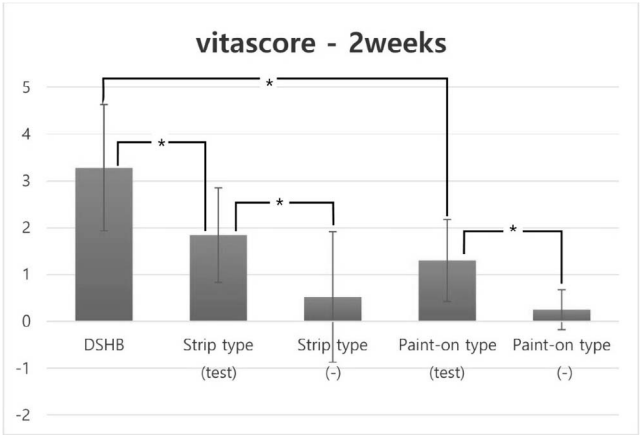

Figure 4. *Vita shade guide: color changes after bleaching for 2 weeks.* *$p<0.05$.

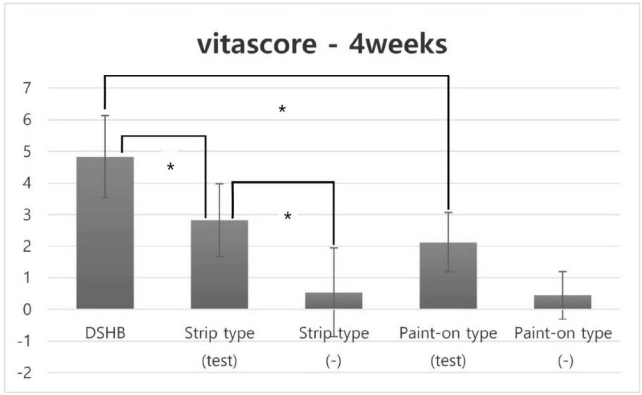

Figure 5. *Vita shade guide: color changes after bleaching for 4 weeks.* *$p<0.05$.

insignificant, because a change in shade is recognized only when ΔE is >3.3.[17] The International Organization of Standardization (ISO) strongly recommends that external tooth-bleaching products show a ΔE of at least 2.[18] In this study, the strip-type and paint-on-type test groups did show considerable tooth color changes. After 4 weeks of bleaching, the color changes were over 2 in all tooth positions, and the mean value was 4.05 in the strip-type group. In the paint-on group, color changes were around 2, and the mean value was 2.12. These results indicate that the strip-type and paint-on-type OTC tooth-bleaching agents caused perceptible color changes, and the values satisfied the recommendations of the ISO.

In this study, there were larger changes in the canines with darker shades. The amount of shade change, from most to least, was in the order of canine, lateral incisor, and central incisor. However, because canines are usually darker than incisors, it is appropriate to consider that there is greater amount of shade change when the tooth has a darker shade, consistent with the findings of previous studies.[8,19,20] A significant correlation was reported between the magnitude of tooth color changes and b* (yellow-blue) values.[20] Thus, teeth of increasingly dark shades of yellow exhibited greater color changes after bleaching.[19]

According to the present study, improvement in shade change was in the order of positive control, strip, and paint-on. After using the bleaching agent for 4 weeks, all test groups showed $\Delta E^* > 2$ overall, indicating significant shade improvement. The strip-type agent was significantly more effective than was the paint-on-type, thus, the null hypothesis was rejected. The strip-type agent showed significant improvement vs the negative control; however, the paint-on-type did not. The color change (ΔE) of the paint-on-type was >2, satisfying the recommendations of the ISO. Similar trends were obtained with the Vita shade guide, although it did not show differences between groups in some tooth positions. Within the limitations of this study, the spectrophotometer appeared superior to the Vita shade guide in detecting differences among groups. Nonetheless, visual assessment is still commonly used because of its convenience and low cost.

The two test products showed inferior results vs the positive control, which could be due to differences in the bleaching agent content (positive control: 10% carbamide peroxide, equivalent to 3.62% H_2O_2[12]; strip-type and paint-on-type: 2.9% H_2O_2); however, consistency and application method could have also affected the results.[21,22] The positive control can be evenly applied on the tooth surface because the bleaching agent has a gel-like consistency. Also, the customized tray minimizes unnecessary contact of the agent with the gingiva and protects the agent from saliva and lip movement. The strip-type agent is designed so that the bleaching agent can be protected from saliva and lip movement. However, it is difficult to apply evenly on the tooth surface, especially because the marginal area of the strip is straight. According to the experimental subjects, the mandibular strip fell off readily from the tooth surface. This could have resulted from saliva affecting retention of the strip and making it difficult for the tooth to be exposed sufficiently to the bleaching agent. Also, a minimal change in shade may have resulted from the smaller amount of the bleaching agent in the strip-type product. The absolute quantity of bleaching agent on the strip was limited. The paint-on-type bleaching agent had a gel-like consistency similar to the positive control, but it was not designed to be

protected from the oral environment as was the positive control and the strip-type product.

Although it is supposed to produce a coating layer when dried, the bleaching agent is thought to be readily removed when in contact with the oral mucosa and to lead to gingival irritation.[7,8] All patients who complained of gingival irritation were in the paint-on-type agent groups. The irritation may not be caused by the H_2O_2, because the same number of patients in both the test and negative control paint-on groups complained of reversible and mild mucosal irritation. Although the paint-on-type had the same H_2O_2 content as the strip-type, it resulted in an inferior shade improvement due to the application method. According to the results, the negative controls also resulted in improvements in tooth shade. This indicates that agents other than H_2O_2 have the potential to change shades.[23] Thus, when investigating the efficacy of a bleaching agent, one should test the product without H_2O_2 rather than use a negative control without any of the components contained in commercially available products to confirm the effect of H_2O_2 concentrations.

Major factors affecting the efficacy of tooth bleaching are concentration of whitening agents and application time.[12,24-27] The degree of color change was smaller in this study, compared with those observed previously. Such differences were due to the lower concentrations of H_2O_2 (2.9%) used in this study, compared with previous studies (6%-10%).[28,29] Higher concentrations of bleaching agents can achieve faster effects but, at least theoretically, when the application time of a product with a lower concentration of bleaching agent is extended, its efficacy can be similar to the highly concentrated bleaching agent. However, practically, it will be difficult to achieve an efficacy similar to a highly concentrated product with a low-concentration product because the relationship between the concentration of bleaching agent and number of applications needed to achieve optimal efficacy have an exponential regression relationship rather than a linear one.[27] In this study, as the use of bleaching agent was repeated, tooth colors were improved but the degree of change decreased.

CONCLUSIONS

- Shade improvement (ΔE) was more than 2 in all test groups, and was in the order of positive control, strip-type, and paint-on-type agent.
- The null hypothesis was rejected because the strip-type was significantly more effective than the paint-on-type.
- However, both OTC tooth-bleaching agents showed significantly lower efficacy than did the dentist-supervised home bleaching kit.
- The tested bleaching agents did not affect PI or GI and caused only minimal and reversible mucosal irritation and hypersensitivity, showing relative safety.

Acknowledgement

This research was supported by a grant (14172MFDS307) from the Ministry of Food and Drug Safety in 2014.

Regulatory Statement

This study was conducted in accordance with all the provisions of the local human subjects oversight committee guidelines and policies of the Ewha Womans University Hospital. The approval code for this study is 14-10A-14.

Conflict of Interest

The authors of this manuscript certify that they have no proprietary, financial, or other personal interest of any nature or kind in any product, service or company that is presented in this article.

(Accepted 24 August 2017)

REFERENCES

1. Haywood VB, & Heymann HO (1989) Nightguard vital bleaching *Quintessence International* **20(3)** 173-176.
2. Park ES, Seong SR, Hong ST, Kim JE, Lee SY, Hwang SY, Lee SJ, Jin BH, Sin HH, & Cho BH (2006) A clinical evalutation of a bleaching strip containing 2.9% hydrogen peroxide *Journal of Korean Academy of Operative Dentistry* **31(4)** 269-281.
3. Demarco FF, Meireles SS, & Masotti AS (2009) Over-the-counter whitening agents: a concise review *Brazilian Oral Research* **23 (Suppl 1)** 64-70.
4. Park DY, Jung SH, Ma DS, Chang SY, & Yun SY (2002) Randomized controlled clinical trial of the efficacy and safety of a 2.6% hydrogen peroxide containing tooth-whitening strips *Journal of the Korean Academy of Dental Health* **26(3)** 385-396.
5. Gerlach RW (2000) Shifting paradigms in whitening: introduction of a novel system for vital tooth bleaching *Compendium of Continuing Education in Dentistry* **(Suppl 29)** S4-S9.
6. Park Y-j, Chung C-p, Hwang S-y, Lee J-k, & Kum K-y (2007) Advanced concept of tooth whitening, 3 : Polymer-based bleaching agents *Dental Success* **27(10)** 1099-1101.
7. Park DY, Ma DS, Cho KM, Jeong DB, & Jeong SH (2005) Efficacy of a paint-on, self-applied, humidity-facilitated setting 2.8% hydrogen peroxide whitening gel *Journal of the Korean Academy of Dental Health* **29(4)** 397-406.

8. Lee JK, Min SH, Hong ST, Oh SR, Shung SH, Hwang YH, You SY, Bae KS, Baek SH, Lee WC, Son WJ, & Kum KY (2009 Clinical study of shade improvement and safety of polymer-based pen type BlancTis Forte whitening agent containing 8.3% carbamide peroxide *Journal of the Korean Academy of Operative Dentistry* **34(2)** 154-161.
9. Jung SH, Park DY, & Ma DS (2004) Efficacy of six months of a 2.6% hydrogen peroxide containing tooth-whitening strips *Journal of the Korean Academy of Dental Health* **28(1)** 117-125.
10. Bernardon JK, Ferrari P, Baratieri LN, & Rauber GB (2015) Comparison of treatment time versus patient satisfaction in at-home and in-office tooth bleaching therapy *J Prosthetic Dentistry* **114(6)** 826-830.
11. Hassel AJ, Koke U, Schmitter M, Beck J, & Rammelsberg P (2005) Clinical effect of different shade guide systems on the tooth shades of ceramic-veneered restorations *International Journal of Prosthodontics* **18(5)** 422-426.
12. Joiner A (2006) The bleaching of teeth: a review of the literature *Journal Dentistry* **34(7)** 412-419.
13. Seghi RR, Johnston WM, & O'Brien WJ (1989) Performance assessment of colorimetric devices on dental porcelains *Journal of Dental Research* **68(12)** 1755-1759.
14. Kielbassa AM, Beheim-Schwarzbach NJ, Neumann K, Nat R, & Zantner C (2009) In vitro comparison of visual and computer-aided pre- and post-tooth shade determination using various home bleaching procedures *Journal of Prosthetic Dentistry* **101(2)** 92-100.
15. Seghi RR (1990) Effects of instrument-measuring geometry on colorimetric assessments of dental porcelains *J Dent Res* **69(5)** 1180-1183.
16. Gross MD, & Moser JB (1977) A colorimetric study of coffee and tea staining of four composite resins *Journal of Oral Rehabilitation* **4(4)** 311-322.
17. Ruyter IE, Nilner K, & Moller B (1987) Color stability of dental composite resin materials for crown and bridge veneers *Dental Materials* **3(5)** 246-251.
18. ISO Standards (2011) *ISO 28399 Dentistry— Products for External Tooth Bleaching* International Organization for Standardization, Geneva, Switzerland.
19. Gerlach RW, & Zhou X (2001) Vital bleaching with whitening strips: summary of clinical research on effectiveness and tolerability *Journal of Contemporary Dental Practice* **2(3)** 1-16.
20. Ishikawa-Nagai S, Terui T, Ishibashi K, Weber HP, & Ferguson M (2004) Comparison of effectiveness of two 10% carbamide peroxide tooth-bleaching systems using spectrophotometric measurements *Journal of Esthetic and Restorative Dentistry* **16(6)** 368-375; discussion 375-366.
21. Ayad F, Giniger M, Proskin HM, Curtis JP, Santarpia PP, Stewart B, DeVizio W, Petrone M, & Volpe AR (2002) Clinical comparison of the stain-removal efficacy of a novel liquid whitening gel containing 18% carbamide peroxide and a commercially available whitening dentifrice *Compendium of Continuing Education in Dentistry* **23(11 Supplement 1)** 18-25.
22. Sagel PA, Odioso LL, McMillan DA, & Gerlach RW (2000) Vital tooth whitening with a novel hydrogen peroxide strip system: design, kinetics, and clinical response *Compendium of Continuing Education in Dentitry* **(29 Supplement)** S10-S15; quiz S42.
23. Niederman R, Tantraphol MC, Slinin P, Hayes C, & Conway S (2000) Effectiveness of dentist-prescribed, home-applied tooth whitening. A meta analysis *Journal of Contemporary Dental Practice* **1(4)** 20-36.
24. Kihn PW, Barnes DM, Romberg E, & Peterson K (2000) A clinical evaluation of 10 percent vs 15 percent carbamide peroxide tooth-whitening agents *Journal of the American Dental Association* **131(10)** 1478-1484.
25. Leonard RH, Sharma A, & Haywood VB (1998) Use of different concentrations of carbamide peroxide for bleaching teeth: an in vitro study *Quintessence International* **29(8)** 503-507.
26. Matis BA, Mousa HN, Cochran MA, & Eckert GJ (2000) Clinical evaluation of bleaching agents of different concentrations *Quintessence International* **31(5)** 303-310.
27. Sulieman M, Addy M, MacDonald E, & Rees JS (2004) The effect of hydrogen peroxide concentration on the outcome of tooth whitening: an in vitro study *Journal of Dentistry* **32(4)** 295-299.
28. Matis BA, Cochran M, Wang G, Franco M, Eckert GJ, Carlotti RJ, & Bryan C (2005) A clinical evaluation of bleaching using whitening wraps and strips *Operative Dentistry* **30(5)** 588-592.
29. Swift EJ, Jr., Heymann HO, Wilder AD Jr, Barker ML, & Gerlach RW (2009) Effects of duration of whitening strip treatment on tooth color: a randomized, placebo-controlled clinical trial *Journal of Dentistry* **37 (Suppl 1)** e51-e56.