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Clinical study on whitening effects and tooth sensitivity of home-whitening agents containing 6% hydrogen peroxide

Shunichi SUDA, Toshiki TAKAMIZAWA, Ryo ISHII, Sho SHIBASAKI, Rei MUTO, Shuhei WATANABE, Ryota AOKI, Soshi SUZUKI and Masashi MIYAZAKI

Department of Operative Dentistry, Nihon University School of Dentistry, 1-8-13 Kanda-Surugadai, Chiyoda-ku, Tokyo 101-8310, Japan
Corresponding author, Toshiki TAKAMIZAWA; E-mail: takamizawa.toshiki@nihon-u.ac.jp

This study aimed to compare the efficacy of tooth whitening and prevalence of tooth sensitivity between 6% hydrogen peroxide (HP) and 10 % carbamide peroxide (CP) at-home whitening systems. Forty-eight patients were chosen and divided into two groups: 6% HP (Tion Take Home With, WI) and 10% CP (Tion Take Home Platinum, PL). Both groups followed the manufacturer's instructions. The whitening procedures were performed over a 10 day period of 1 h per day in WI and a 14 day period of 2 h per day in PL. Tooth color changes were measured with a spectrophotometer. The pain intensity was assessed using a numerical rating scale. No significant differences in ΔE^*ab, ΔE_{00}, and ΔW_{ID} were found between the groups. Tooth sensitivity was more prevalent in WI than in PL. Ten days of 6% HP use was as effective as 14 days of 10% CP.

Keywords: Tooth whitening, At-home whitening, 6% hydrogen peroxide, Whitening interval

INTRODUCTION

Patient interest in tooth color is associated with a growing demand for treatments that improve tooth esthetics. Many patients with discolored teeth seek optimal whitening treatments to improve their dental esthetics[1]. Vital tooth whitening improves patients' oral health-related quality of life, allowing them to smile and display their teeth without feeling embarrassed[2]. Among teeth-whitening techniques, at-home whitening that employs customized trays is more adaptable than in-office whitening because it is simpler and cheaper, and involves less chair time than in-office whitening[3] despite having the same whitening effect as the latter[4]. New whitening systems have continued to be developed, and a variety of products are available at present.

The most commonly reported side effect after whitening is tooth sensitivity caused by whitening agents[5]. Tooth sensitivity during and after whitening procedures is generally mild and transient; however, sometimes it is severe and irritating, causing patients to abandon whitening treatments[6]. The investigated incidence of tooth sensitivity varies significantly in the literature, and the wide range of individual differences and available whitening agents makes it hard to accurately evaluate the degree of sensitivity. In order to mitigate the incidence of tooth sensitivity, researchers have tried adding desensitizers to whitening products; however, they have failed to significantly reduce the severity of sensitivity using this method[7]. Currently, the main focus is to mitigate the tooth sensitivity risk by using whitening products at lower concentrations, increasing the intervals between whitening cycles, and reducing the interval of whitening product use while still maintaining effective whitening results.

New whitening systems have continued to be manufactured, making it difficult to organize or clearly understand the concept of whitening, especially as a variety of products is available. Among them, at-home whitening using 10% carbamide peroxide (CP) and custom-made trays is thought as the gold standard for treating discolored teeth because of its low tooth sensitivity risk and trustworthy whitening effect[8]. On the flip side, at-home whitening is a more time-consuming method that requires daily use for several weeks to obtain a satisfactory whitening effect[9]. Several improvements have been made to whitening technology as changes have been made in the active ingredient concentration, interval of custom tray use, and active ingredient type. Several changes were envisioned to shorten the interval required to achieve a satisfactory color change, including increasing the active CP gel concentration and introducing a low hydrogen peroxide (HP)-based at-home whitening product.

Recently, an at-home whitening agent containing 6% HP using custom trays has been launched commercially in Japan. This product, which is worn on custom trays for 60 min per day for 10 days, is characterized by its efficient whitening effect exerted over a relatively short period. Furthermore, the manufacturer claims that the whitening agent is easily absorbed by water, allowing the active ingredients to penetrate the tooth surface and resulting in efficient whitening. However, to our knowledge, there is limited information available on the impact of this new type of at-home whitening agent on the whitening efficacy and tooth sensitivity risk when compared to the conventional at-home whitening systems with 10% CP. It would also be instrumental to understand the impact of a shorter at-home whitening interval on the whitening efficacy and tooth sensitivity prevalence.

This clinical study aimed to investigate the

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whitening efficacy and tooth sensitivity of prevalence of a new at-home whitening system containing 6% HP, and compared it to a conventional at-home whitening system containing 10% CP. The null hypotheses to be tested are: i) the efficacy of tooth whitening would not differ between the at-home whitening systems; ii) the tooth sensitivity prevalence would not differ between the at-home whitening systems.

MATERIALS AND METHODS

Study materials, ethical approval, and trial registration
The protocol of this clinical investigation was evaluated and approved by the Ethics Committee for Human Studies at Nihon University School of Dentistry (EP24D002) before the study began. In addition, this clinical investigation was registered in the Japanese clinical trial database (University Hospital Medical Information Network, UMIN000056501). For the at-home whitening systems, 6% HP (Tion Take Home With, WI; GC, Tokyo, Japan), and 10% CP (Tion Take Home Platinum, PL; GC) were used. The whitening systems used in this study are shown in Table 1.

Sample size calculation
A statistical software program (G* Power, Heirich-Heine-Univertät Düsseldort, Düsseldorf, Germany) was used to determine the minimum required sample size, and it was indicated that at least 15 patients in each group were needed for an efficient study. Considering the estimated dropout rate of patients undergoing whitening treatment, it was determined that the study would require a minimum of 20 initial participants. Ultimately, 24 participants were included in each group.

Experimental design (inclusion and exclusion criteria)
Informed consent for inclusion in the study was given by all participants. Forty-eight participants (29 women and 19 men) were included. The participants in the WI and PL groups had an average age of 24.4 years and 23.3 years, respectively (Table 2). The inclusion and exclusion criteria for this study were based on those of our previous whitening clinical investigations[10,11].

Blinding and randomization
The present study was a parallel clinical trial. Operators, evaluators, and participant consultants were blinded to group assignment. Four board-certified (Japanese Society of Conservative Dentistry) dentists with at least five years of relevant clinical experience were recruited as operators. Additionally, two board-certified dentists, also with more than five years of relevant clinical experience, were recruited as evaluators. In addition, the operator, evaluator, participant consultant, and statistician were separate dentists who did not fill more than one role. Forty-eight eligible participants were randomly divided into two groups with different at-home whitening procedures. The randomization process involved filling out sequentially numbered cards with details of the assigned groups and sealing them in envelopes that were opened by the operator to determine group assignment after participant eligibility was confirmed and baseline assessments were completed.

Whitening procedure
A schematic protocol for at-home whitening and color tone measurements is shown in Fig. 1. Forty-eight participants were randomly assigned to two groups of 24 (the WI and PL groups) with different whitening protocols. Whitening was performed on six maxillary anterior teeth and two premolars. Participants in the WI group were indicated to wear trays containing whitening agents for 1 h per day for 10 consecutive days as per the manufacturer's instructions. After 10 days of active treatment, the participants were recalled and the information recorded at baseline was updated during the post home whitening visit. In the PL group, participants were advised to wear custom trays containing whitening agents for 2 h per day for 14 consecutive days, again as per the manufacturer's instructions. After the active whitening treatment, the participants were recalled and the information recorded at baseline was updated.

Table 1 Materials used in this study

Code	Home whitening system (Lot. No)	Main components	Directions	Manufacturer
WI	Tion Take Home With (2403061)	Hydrogen peroxide 6%, polyalcohol, viscosity modifier, pH modifier	Once a day for 60 min for 10 days	GC, Tokyo, Japan
PL	Tion Take Home Platinum (2405171)	Carbamide peroxide 10%, polyalcohol, viscosity modifier, pH modifier	Once a day for 120 min for 14 days	GC

Table 2 Distribution and characteristics of subjects in this study

Group	Age	Sex
WI	24.4 (4.0)	Male: 10/Female: 14
PL	23.3 (3.0)	Male: 9/Female: 15

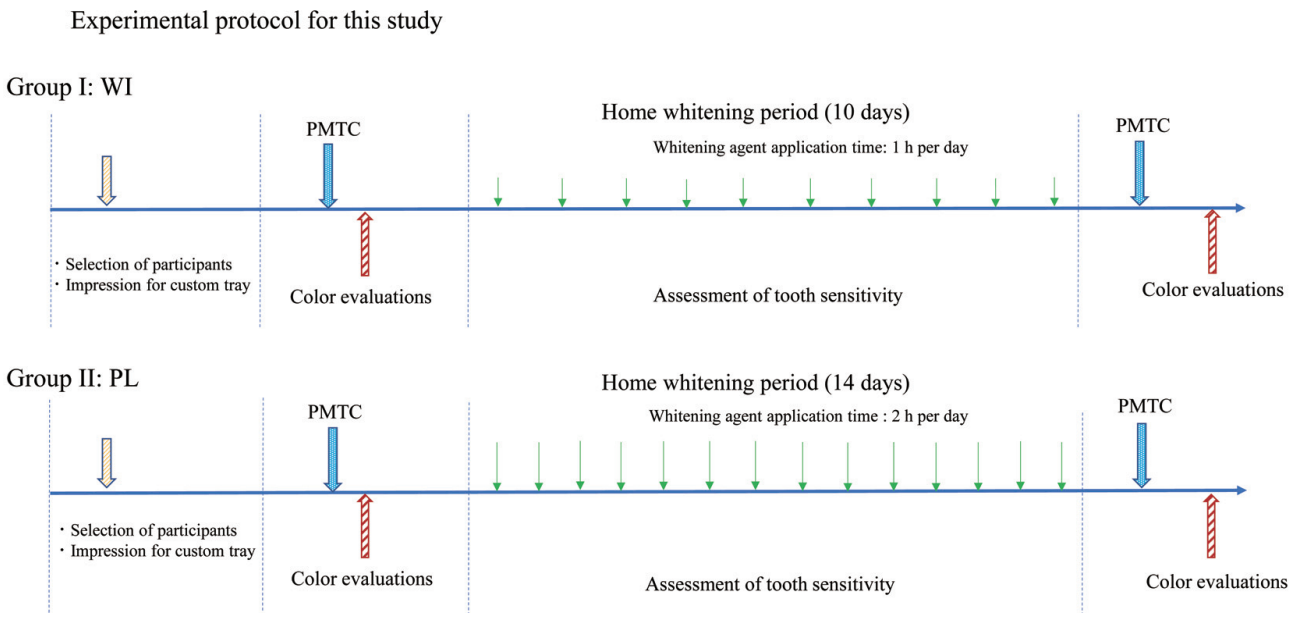

Fig. 1 Experimental protocol for this study.

Personal information was recorded at the initial visit, and all patients underwent professional teeth cleaning with a prophy paste (MERSAGE FINE, Shofu, Kyoto, Japan) using a toothbrush (MERSAGE Brush No. 1, Shofu) to remove exogenous stains. Impressions were made on the maxillary arch of each participant with alginate (Aroma Fine Plus, GC), disinfected, and filled with dental stone (New Plastone II, GC). The model was cut into a horseshoe shape, and a vacuum machine (Erkopress ci motion, Erkodent Erich Kopp, Pfalzgrafenweiler, Germany) was used to apply 1-mm-thick hydrogenated styrene-isoprene block copolymer material (Tion Take Home Tray Sheets, GC) to create customized trays without reservoirs. The surplus material on the labial and lingual sides was trimmed to fabricate scallop-cut trays. At this point, grouping was unveiled and each patient was given a custom tray and home medication.

Assessment of the whitening effect

Tooth color changes were assessed before and after at-home whitening using a dental spectrophotometer (Crystaleye, Olympus, Tokyo, Japan). All measurements were performed by two trained operators working in the same standardized test environment. The same evaluator assessed the color changes of the each patient before and after whitening. The equipment was calibrated before each measurement. The spectrophotometer head was fitted with a disposable contact cap, and the instrument was then positioned near the center of the right maxillary incisor before images of the teeth were taken. The reflectance spectra of the center of the right anterior incisor were analyzed.

The Commission International de l'éclairage (CIE) L^*, a^*, and b^* coordinates were obtained for the tooth's central areas. The color change ($\Delta E/\Delta E_{00}$) and whitening indices (ΔW_{ID}) were determined based on the previous studies[10-12].

Assessment of tooth sensitivity

The numerical rating scale (NRS) was employed to evaluate the intensity of tooth sensitivity experienced during at-home whitening procedures and for a period of up to 24 h thereafter. On the NRS, numbers from 0 to 10 are evenly distributed throughout the page, with "0" indicating no pain and "10" indicating the worst pain possible. Participants are instructed to circle the number representing the intensity of the pain they are experiencing during the assessment. In addition, the absolute risk of tooth sensitivity due to whitening is equivalent to the sum of the percentages of participants who had tooth sensitivity at least once during the active whitening treatment, or up to 24 h after whitening was calculated. The same evaluator assessed the tooth sensitivity of the each patient before and after whitening, as for the color measurements.

Statistical analysis

The Brown-Forsythe and Shapiro–Wilk tests were selected to check for equality of variance and normality, respectively, for each data set. The Shapiro–Wilk test showed that none of the data sets were statistically normal ($p<0.05$). Therefore, nonparametric analyses were used. The tooth color change, absolute risk of tooth sensitivity, and intensity of tooth sensitivity (based on the NRS) were compared between the two groups using the Mann–Whitney U test ($\alpha=0.05$).

RESULTS

Whitening efficacy

Spectrophotometric analysis results of ΔE^*ab, ΔE_{00}, ΔW_{ID}, ΔL^*, Δa^*, and Δb^* between before and after at-home whitening are shown in Tables 3, 4 and Figs. 2, 3. There were no significant differences in color variation [ΔE^*ab (p=0.718) and ΔE_{00} (p=0.869) and ΔW_{ID} (p=0.445)] between the two whitening groups. Both whitening groups showed increased L^* values after whitening compared with prewhitening values. However, ΔL^* values did not differ significantly between the WI and PL groups (p=0.563). The a^* and b^* values both decreased after whitening in the two groups. No significant differences in Δa^* (p=0.984) and Δb^* (p=0.996) were observed between the two whitening groups as for the ΔL^*.

Tooth sensitivity

The absolute tooth sensitivity risk and average tooth sensitivity intensity are shown in Tables 5, 6 and Fig. 4. For the WI group, the absolute risk of tooth sensitivity

Table 3 Spectrophotometric analysis of ΔE^*ab, ΔE_{00}, and ΔW_{ID} between before and after home whitening (Medians and interquartile ranges)

	ΔE^*ab	ΔE_{00}	ΔW_{ID}
WI	3.82 (2.58/5.47)[a] (95% CI: 3.40, 5.02)	2.62 (1.85/3.70)[a] (95% CI: 2.33, 3.48)	5.27 (8.22/4.07)[a] (95% CI: 4.77, 8.20)
PL	3.75 (2.33/6.40)[a] (95% CI: 3.09, 5.00)	2.70 (1.55/4.30)[a] (95% CI: 2.21, 3.57)	5.19 (7.89/1.97)[a] (95% CI: 3.81, 7.25)

Same lower case letter in columns indicates no difference at 5% significance level.
CI: confidence interval
Unlabeled values in parenthesis indicate standard deviation.

Table 4 Spectrophotometric analysis of ΔL^*, Δa^*, and Δb^* between before and after home whitening (Medians and interquartile ranges)

	ΔL^*	Δa^*	Δb^*
WI	−2.13 (−3.21/−1.21)[a]	0.67 (0.40/1.05)[a]	2.86 (2.07/3.98)[a]
PL	−2.34 (−4.25/−0.9)[a]	0.82 (−0.13/1.36)[a]	2.06 (1.04/3.68)[a]

Same lower case letter in columns indicates no difference at 5% significance level.
Same capital letter in rows indicates no difference at 5% significance level.
Values in parenthesis indicate standard deviation.

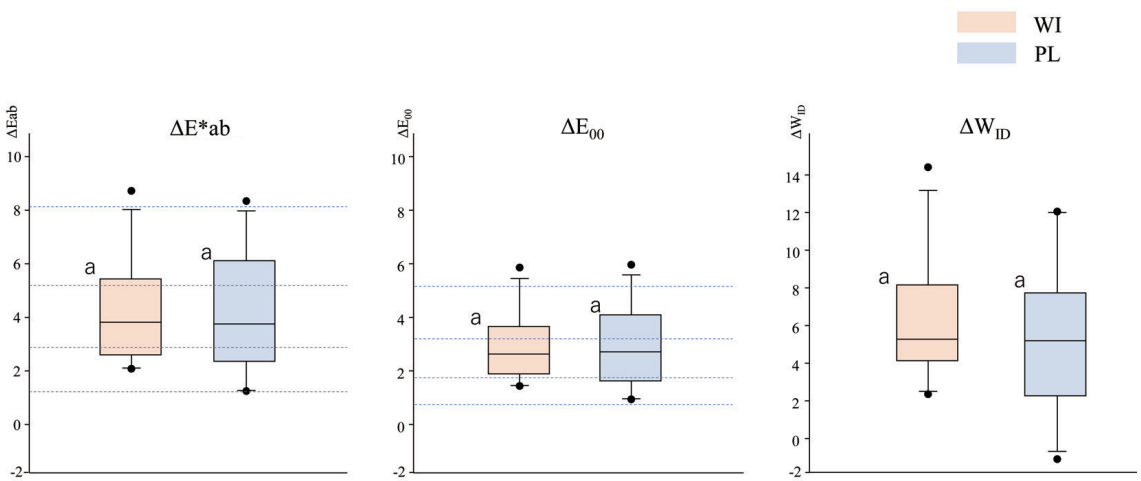

Fig. 2 Spectrophotometric analysis of ΔE^*ab, ΔE_{00}, and ΔW_{ID}.
Same lower case letter indicates no difference at 5% significance level. Interpretation of whitening-dependent color differences through PT and AT; Moderate effectiveness: ΔE^*ab (>1.2, ≤2.7), ΔE_{00} (>0.8, ≤1.8), Good effectiveness: ΔE^*ab (>2.7, ≤5.4), ΔE_{00} (>1.8, ≤3.6), Very good effectiveness: ΔE^*ab (>5.4, ≤8.1), ΔE_{00} (>3.6, ≤5.4).

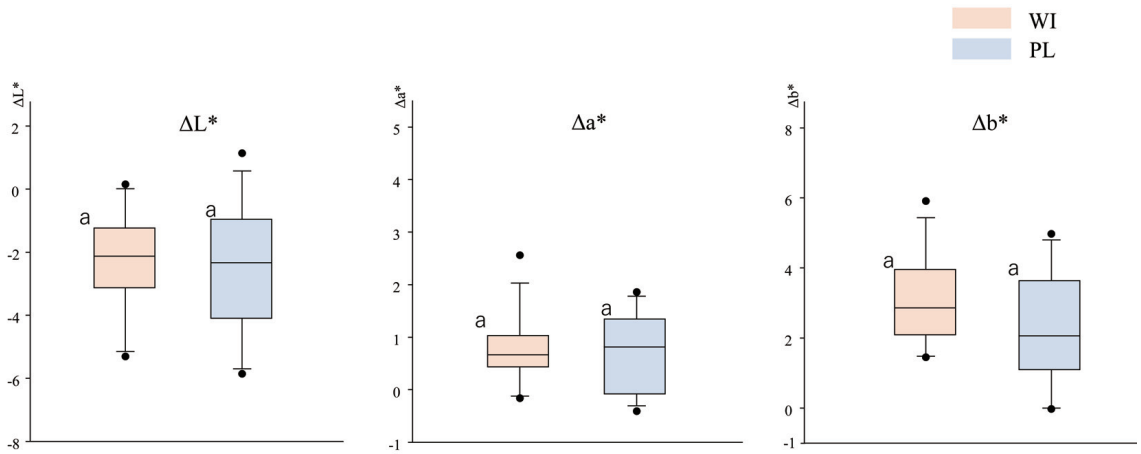

Fig. 3 Spectrophotometric analysis of ΔL^*, Δa^*, and Δb^*.
Same lower case letter indicates no difference at 5% significance level.

Table 5 Absolute risk for tooth sensitivity through the whitening treatment

	During treatment	Up to 24 h after treatment
WI	80/240 (33.3%)	77/240 (32.1%)
PL	75/336 (22.3%)	66/336 (19.6%)

Absolute risk: Cumulative number of people who felt tooth sensitivity at least once/total whitening days

Table 6 Average intensity of tooth sensitivity: NRS values and standard deviations

	During treatment	Up to 24 h after treatment
WI	0.83 (1.28)aA (95% CI: 0.32, 1.34)	1.03 (1.76)aA (95% CI: 0.32, 1.73)
PL	0.99 (1.89)aA (95% CI: 0.24, 1.74)	0.71 (1.71)aA (95% CI: 0.03, 1.39)

Same lower case letter in columns indicates no difference at 5% significance level.
Same capital letter in rows indicates no difference at 5% significance level.
Unlabeled values in parenthesis indicate standard deviation.
CI: confidence interval

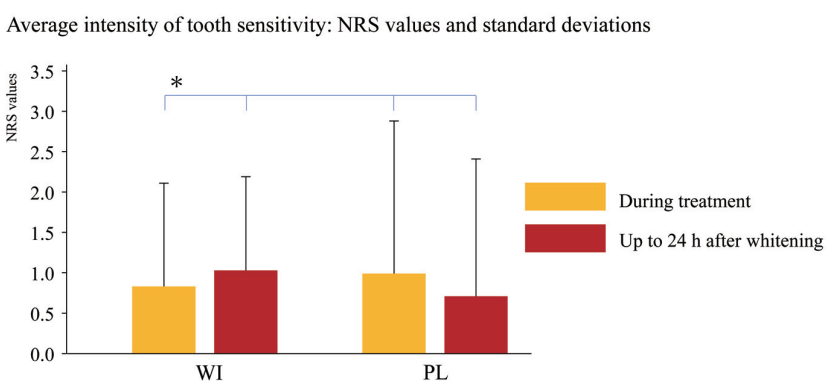

Fig. 4 Average intensity of tooth sensitivity.
Asterisk indicates no difference at 5% significance level.

during treatment did not differ significantly from that up to 24 h after treatment (p=0.999). The WI group showed a higher absolute risk than the PL group during treatment and up to 24 h after treatment. The average tooth sensitivity intensity, both during treatment and up to 24 h after treatment, did not differ significantly between the WI and PL groups; furthermore, this parameter during treatment did not differ significantly from that up to 24 h after treatment in both groups (p=0.110).

DISCUSSION

In this study, the whitening period and application time of the whitening agent were different in the protocols for WI and PL as the manufacturer's instructions were followed. The total time for which the teeth were exposed to the whitening agent in WI was approximately one third that in PL. The results do not, therefore, allow a direct comparison of the whitening materials, but rather compare the treatments, as specified by the manufacturer. In this study, no significant differences were observed in ΔE^*ab, ΔE_{00}, and ΔW_{ID} between the WI and PL groups after the completion of at-home whitening, nor were there any significant differences in ΔL^*, Δa^*, and Δb^*. These results suggested that at-home whitening with 6% HP in the present study can improve color faster than at-home whitening with 10% CP. Thus, although the first null hypothesis, "no difference in the whitening effect of different home whitening agents," was not rejected, a significant difference in the time to achieve the whitening effect was observed. Although both HP and CP are used as whitening agents, their properties should differ significantly. A previous systematic review and meta-analysis of the at-home whitening effects of CP and HP found that CP gel had a slightly better whitening effect than HP-based products with respect to ΔE; however, this finding should be interpreted cautiously since the changes in shade guide unit data did not differ significantly among products[13].

There is a growing demand for the quantification of tooth color, whiteness, and perception[13]. Dental professionals traditionally evaluate tooth color using shade guides that provide a reference standard for visual comparison[14]. However, it is difficult to ensure consistency among different human raters due to lighting variations, experience, age, human eye fatigue, and visual acuity[15]. Instead, tooth color measurement using instruments such as colorimeters, spectrophotometers, spectroradiometers, and digital cameras has been widely practiced. Color measurements by instruments are usually expressed in terms of CIE XYZ tristimulus values or CIELAB values. In the CIELAB system, the variable L^* represents the lightness difference (L^*=100) and darkness difference (L^*=0), while the variables a^* and b^* represent the color values on the red-green and yellow-blue axes, respectively[16]. In dentistry, both systems are widely used to assess tooth whiteness. However, it is not easy to relate changes in $L^*a^*b^*$ and XYZ values to changes in perceived whiteness.

The CIELAB formula has recently evolved into the CIEDE2000 formula and ΔE^*ab is now ΔE_{00}. According to CIE Technical Report 142-2001 ΔE_{00}, it can be calculated from three parameters (hue, saturation, and lightness) and is said to represent values closer to human color discrimination than conventional color difference measurements[17]. Therefore, ΔE_{00} is said to represent a value closer to human color discrimination than conventional colorimetry. ΔE_{00} not only considers saturation, hue, lightness, and weighting functions as well as hue difference and saturation, and between blue and gray performance. It was reported that the CIELAB 50:50% perceptibility threshold (PT) was ΔE^*ab=1.2, whereas the 50:50% 0:50% acceptability threshold (AT) was ΔE^*ab=2.7. The corresponding CIEDE2000 (ΔE_{00}) values were 0.8 and 1.8, respectively[18]. In this study, the WI and PL groups showed ΔE^*ab of more than those values after at-home whitening, which indicated the effectiveness of whitening in both groups (Fig. 1).

Appropriate whiteness measurement and color assessment are critical in the investigation and manufacture of dental materials and in clinical scenarios, such as evaluating the efficacy of different whitening agents and determining the degree of clinical success of clinical whitening treatments. This trend is promoting the development of new whiteness indices for dental applications based on the CIELAB color space[19]. In this study, the W_{ID} was used to evaluate the visual threshold of whiteness. The use of an appropriate whiteness index is critical because it allows for better correlations of visual judgments to instrumental whiteness difference values. Thus, the W_{ID} is considered a CIELAB-based index that has been validated under laboratory and clinical conditions and developed specifically for assessing whiteness in dentistry, surpassing previous indices[20]. According to the findings of previous studies, the PT and AT for W_{ID} are 0.72 and 2.60, respectively[21]. Therefore, a change in whiteness that exceeds 0.72 W_{ID} units would be perceived by the average observer. The visual whiteness difference threshold determined using the W_{ID} index was considered useful as a reference value in a series of clinical practice situations, such as the effective evaluation of whitening agents in dentistry and color studies[22].

The PL used in this study is composed mainly of 10% CP, the equivalent of 3.35% HP[23], which is a lower HP concentration than that of WI. On the other hand, the custom tray application duration was 2 h per day for 14 days for PL (total exposure time is 28 h) and 1 h per day for 10 days for WI (total exposure time is 10 h). The main factors affecting the effectiveness of teeth whitening are the concentration of the whitening agent and the application duration[24]. In the present study, there was no significant difference in whitening efficacy between different HP concentrations, probably because of differences in whitening material systems and application durations. Although a higher whitening agent concentration produces a more rapid effect (at least theoretically), a product with a lower whitening agent concentration would have a longer application

duration and therefore would be as effective as a product with a higher whitening agent concentration. However, a previous report indicated that the overall evidence generated was so low in certainty that no solid conclusions could be drawn regarding the superiority of the whitening compositions or the specific application method, concentration, application duration, or interval of application[25]. Therefore, further studies are considered necessary.

For tooth sensitivity during and after at-home whitening, the absolute risk and average intensity of tooth sensitivity in this study tended to be higher in the WI group than in the PL group. Thus, the second null hypothesis that the prevalence of tooth sensitivity in at-home whitening does not differ with the type of whitening material was rejected. Tooth sensitivity due to whitening is the most common side effect reported by patients undergoing whitening procedures, even when at-home whitening is applied[26]. Tooth sensitivity, which may occur early in the whitening process, generally ceases in most patients 24–48 h after the whitening process ends[27]. The incidence of tooth sensitivity varies considerably in the published literature, and it is difficult to accurately assess the degree of sensitivity due to individual differences and the wide range of available whitening agents. Tooth sensitivity occurs because of the low molecular weight of HP, which results in faster penetration of the dentinal structure and facilitates the penetration of the pulp chamber[28]. Higher HP concentrations result in increased enamel permeability and the release of more free radicals that will reach the pulp[29]. In an attempt to reduce the occurrence of tooth sensitivity, manufacturers have tried adding desensitizers to whitening products but reported that they did not significantly reduce the risk or severity of tooth sensitivity[30]. Currently, the main approach is to minimize the tooth sensitivity risk by using lower concentrations of whitening products, increasing the interval between whitening cycles, and shortening the interval of use, while ensuring effective whitening efficacy. In this regard, WI contains 6% HP but with a shorter wearing duration of 60 min per application and an interval of 10 days, considering the reduced incidence of tooth sensitivity.

The absolute risk and mean intensity of tooth sensitivity were not significant during whitening and up to 24 h after whitening, regardless of the home whitening group. Postwhitening hypersensitivity is characterized by a delayed incidence of hypersensitivity, which occurs during whitening and up to 24 h postwhitening. Interviews regarding postwhitening tooth sensitivity have indicated that many participants experienced short and sharp pains regardless of external stimulation. Although this study did not directly investigate the mechanisms of postwhitening tooth sensitivity, we need to consider the possibility that these mechanisms may differ from those proposed by long-standing theories of dentin hypersensitivity. Recent studies have suggested that it would be difficult to explain the occurrence of tooth sensitivity due to whitening with a hydrodynamic theory and that an ion channel protein, transient receptor potential ankyrin 1 (TRPA1), is likely to be involved[31]. This new model of tooth sensitivity known as the odontoblast hydrodynamic receptor theory[32] awaits further investigation as it may explain postwhitening tooth sensitivity.

One of the limitations of the current study was that most participants were from the younger generation and female. This may affect the generalizability of the outcome of the investigation to the overall population. Furthermore, the investigation of the efficacy of at-home whitening was conducted after a brief period. Consequently, the color stability of different at-home whitening agents remains uncertain, further research is needed to evaluate color stability over an extended period of time. Although this study showed promising results for whitening materials containing 6% HP, more clinical studies should be conducted to evaluate the clinical efficacy and side effects of shorter application durations and lower-HP-concentration protocols for at-home whitening.

CONCLUSION

At-home whitening with 6% HP had a faster whitening effect than that with 10% CP. Tooth sensitivity during and after whitening tended to be higher with 6% HP than with 10% CP, which was presumably due to the higher HP concentration.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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