

Randomized Double-blind Clinical Trial of Bleaching Products in Patients Wearing Orthodontic Devices

A Montenegro-Arana • LA Arana-Gordillo • D Farana
A Davila-Sanchez • E Jadad • U Coelho
OMM Gomes • AD Loguercio

Clinical Relevance

Bleaching products based on 8% and 10% hydrogen peroxide concentrations can be effective alternatives for dental bleaching in patients with fixed orthodontic appliances.

SUMMARY

Objectives: This double-blind randomized clinical trial evaluated tooth sensitivity (TS) and the effectiveness (EF) of two types of bleaching agents (Trèswhite Ortho [TWO] and Trèswhite Supreme [TWS]) when used in patients wearing orthodontic appliances.

Methods and Materials: Forty patients between the ages of 18 and 40 years were ran-

domly stratified, with an equal allocation rate, into two groups (n=20), according to the bleaching agent applied. Tooth color of the six maxillary anterior teeth was measured before and after the treatment with a spectrophotometer. The TS was recorded on three scales before and during the bleaching treatment.

Results: With regard to EF, a significant reduction was found (ranging from 7.3-9.6 and 5.3-9.5 Vita scale units for TWO and

Andres Montenegro-Arana, DDS, MS, PhD student, Department of Restorative Dentistry, Ponta Grossa State University, Restorative Dentistry, Ponta Grossa, Brazil

Luis Alfonso Arana-Gordillo, DDS, MS, PhD, University of Santiago de Cali, Restorative Dentistry, Santiago de Cali, Colombia

Diana F. Arana, DDS, MS, University of Santiago de Cali, Restorative Dentistry, Santiago de Cali, Colombia

Andres Davila-Sanchez, DDS, MS, PhD student, professor, Ponta Grossa State University/San Francisco de Quito University, Ponta Grossa, Brazil

Enrique Jadad, DDS, MSc, Santiago de Cali University, Restorative Dentistry, Barranquilla, Colombia

Ulisses Coelho, DDS, MS, PhD, Department of Restorative

Dentistry, Ponta Grossa State University, Restorative Dentistry, Ponta Grossa, Brazil

Osnara Maria Mongrue Gomes, Department of Restorative Dentistry, Ponta Grossa State University, Restorative Dentistry, Ponta Grossa, Brazil

*Alessandro D Loguercio, DDS, MS, PhD, Department of Restorative Dentistry, Ponta Grossa State University, Restorative Dentistry, Ponta Grossa, Brazil

*Corresponding author: Rua Carlos Cavalcanti, 4748, Bloco M, Sala 64A – Uvaranas, Ponta Grossa, PR 84030-900, Brazil; e-mail: aloguercio@hotmail.com

DOI: 10.2341/15-240-C

TWS, respectively, $p < 0.001$); however, there was no statistical difference between the groups ($p > 0.63$). The number of patients with sensitivity was 58.8% and 73.3% for TWO and TWS groups, respectively ($p = 0.53$); however, with each of the three scales used, the intensity of sensitivity was low and there was no statistical difference between TWO and TWS ($p > 0.05$).

Conclusions: In spite of producing a side effect of low TS, the two bleaching treatments tested were effective for dental bleaching in patients with fixed orthodontic appliances.

INTRODUCTION

Tooth bleaching is one of the most requested dental procedures nowadays. It is commonly chosen as the first option to improve tooth color because it is considered a minimally invasive approach compared with other esthetic procedures, such as crowns or veneers.¹ Dental bleaching can be performed directly by the dentist at the clinic (in-office bleaching), by the patient at home with professional supervision (at-home bleaching), or by the patient without professional supervision with over-the-counter products (over-the-counter).

As a result of its relative ease of use, low cost, safety, and acceptance by patients, at-home dental bleaching has gained great popularity² among dentists and patients. More recently these benefits were extended to the orthodontic field as a complementary treatment.^{3,4} The use of these bleaching agents during orthodontic treatment is of great importance, because this treatment will allow the final esthetic result of the teeth and the smile to be additional goals of the orthodontic treatment process.⁵⁻⁸

The attempt to bleach teeth "covered" by restorative materials⁹ or with orthodontic appliances^{3,4} is not new, but it is only recently that a new product has become available on the market: Opalescence Trèswhite Ortho (TWO, Ultradent, Opal Orthodontics Inc, South Jordan, UT, USA). This product has been developed to meet the esthetic needs of patients wearing orthodontic appliances before the appliances are removed. This specific product was evaluated in a published clinical trial.³ In this study, patients with or without brackets and appliances were subjected to tooth bleaching with a preloaded flexible tray containing 8% hydrogen peroxide (TWO), which had to be kept on the teeth (without brackets) or on the brackets/teeth for

approximately 45 minutes to achieve adequate contact time between the whitening gel, teeth, and brackets. After 10 days, the results showed TWO to be an efficient bleaching agent in patients wearing fixed orthodontic appliances, with results similar to those found in the group that did not wear any appliances.

Recently a published case report⁴ described the use of Opalescence Trèswhite Supreme (TWS, Opal Orthodontics, Ultradent Products), a product containing 10% hydrogen peroxide, in a patient with brackets. Although the manufacturer did not indicate that this product was designed for the purpose of use with orthodontic appliances, the results of this report showed a good pattern of bleaching. Unfortunately, in spite of the good clinical results in terms of bleaching effectiveness, these two articles^{3,4} did not include any comments with regard to tooth sensitivity.

Tooth sensitivity is the most common side effect associated with use of at-home bleaching or over-the-counter products with high concentrations. Typically more than 70%^{1,10-12} of patients report sensitivity, with levels ranging from very mild to intolerable.¹³ It is known that the diffusion of hydrogen peroxide through tooth structures depends on the initial concentration of the bleaching agent.¹³⁻¹⁵ When different bleaching agent concentrations are used in at-home/over-the-counter techniques, in general, those with higher concentrations produce higher levels of sensitivity.^{1,10-12}

In view of the foregoing, the primary objective of this study was to evaluate the tooth sensitivity induced by over-the-counter bleaching agents with different concentrations when applied in patients with orthodontic appliances, considering that as far as we know, no previous randomized clinical trials have addressed this question. Moreover, since the main difference between TWO and TWS is the gel concentration, these products were chosen for this randomized clinical trial. The second aim of this investigation was to evaluate the clinical effectiveness of the above-mentioned two over-the-counter bleaching agents with different concentrations when applied in patients with orthodontic appliances. The following null hypotheses were tested in this study: 1) the color change is the same for both of the over-the-counter bleaching agents with different concentrations, and 2) no difference in tooth sensitivity is observed between the over-the-counter bleaching agents with different concentrations.

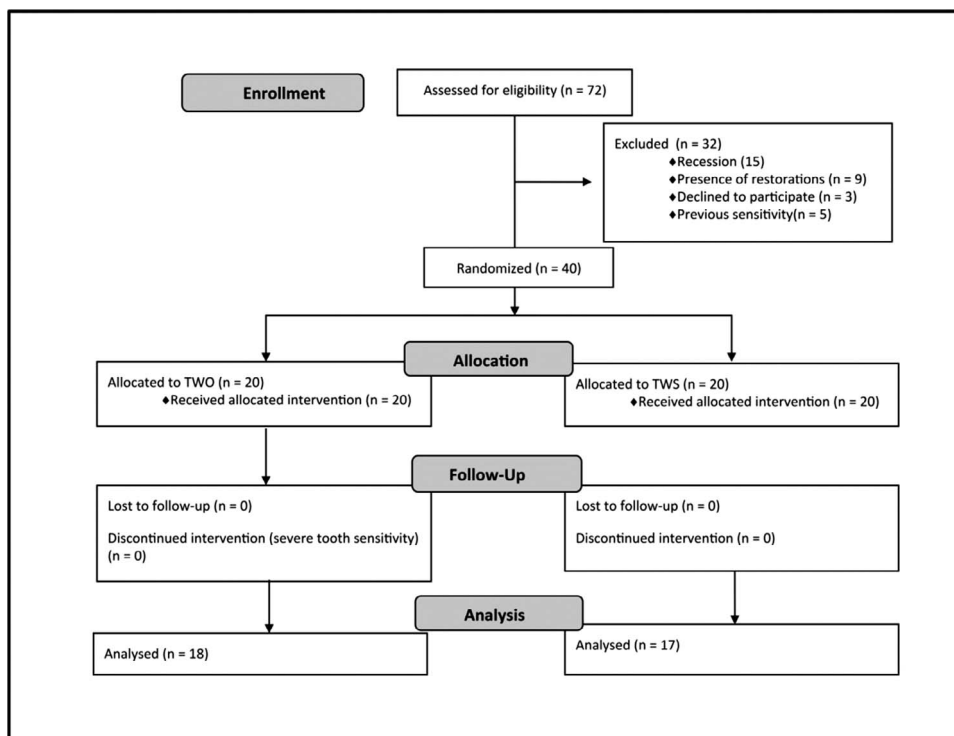


Figure 1. Flow diagram of the clinical trial including detailed information on the excluded participants.

METHODS AND MATERIALS

Study Design

This clinical investigation was approved (Protocol 19033/10) by the scientific review committee and by the committee for the protection of human subjects of the local university. The experimental design was based on the guidelines of the CONSORT statement.¹⁶ This was a randomized, double-blind clinical trial with an equal allocation rate to receive either one of two treatments. Once the criteria were established, 40 volunteers were selected for this study.

Inclusion and Exclusion Criteria

Patients included in this clinical trial were at least 18 years of age or older and had good general and oral health. A total of 72 participants were examined in a dental chair to check whether they met the inclusion and exclusion criteria (Figure 1). The participants needed to be using orthodontic appliances. The requirement was to present six caries-free maxillary anterior teeth, without restorations on the labial surfaces, and these teeth had to be shade A3 or darker. Participants who had undergone previous tooth-whitening procedures, presented anterior restorations, were pregnant/lactating, or who had severe internal tooth discoloration (tetracycline

stains, fluorosis, pulpless teeth), spontaneous sensitivity, bruxism habits, or any other pathology that could cause tooth sensitivity (such as recession, exposed dentin) were excluded from the study since they would not be eligible for cosmetic treatment such as bleaching.

Sample Size Calculation

The sample size calculation was based on the absolute risk of tooth sensitivity, the primary outcome of the study. Forty patients (20 in each group) were required to have an 80% chance of detecting a decrease in the primary outcome measure from 66% (mean absolute risk of tooth sensitivity, based on high-concentration at-home bleaching gels^{1,10-12} in the TWS group to 25% in the TWO group [$\alpha=0.05$]). The sample size was calculated using the Website www.sealedenvelope.com. The present study was powered to detect a high significant effect.

Subject Allocation

The 40 participants were randomly allocated to the TWO and TWS groups (Table 1). As the over-the-counter products are very similar in terms of presentation and manufacturer recommendations, the patients were considered blind. The participants

Table 1: *Details of the Bleaching Agents Used*

Bleaching Agent/Manufacturer	Hydrogen Peroxide, %	Application Time	Composition*	Batch No.
Trèswhite Ortho (TWO)/Ultradent	8	45 min/10 d	Carbamide peroxide 7.5%; hydrogen peroxide 7.5%; sodium fluoride 0.25%, and sodium hydroxide 3.75%	68561.1
Trèswhite Supreme (TWS)/Ultradent	10	45 min/10 d	Carbamide peroxide 7.5%; hydrogen peroxide 3%-13%; sodium fluoride 0.25%, and sodium hydroxide <5%	85007.2

* Data provided by the manufacturer.

were randomly divided in the two groups (TWO or TWS). A third operator, not involved in the research protocol, conducted the randomization process, which recorded the details of the allocated groups on cards placed in sequentially numbered, opaque and sealed envelopes. Once the participant was eligible for the procedure and completed all baseline assessments, the operator could open the envelope. Neither the participant nor the operator knew the group allocation before this stage.

Shade Evaluation

Shade evaluation was recorded before the procedure and 30 days after finishing the bleaching treatment using an objective evaluation (spectrophotometer Easyshade, Vident, Brea, CA, USA); the spectrophotometer was calibrated before and after the procedure. For this evaluation, a preliminary impression of the maxillary arch was made using dense silicone Adsil (Vigodent S/A Indústria e Comércio – Rio de Janeiro, RJ, Brazil). The impression was extended to the maxillary canine and served as a standard color measurement guide for the spectrophotometer. A window was created on the labial surface of the molded silicone guide in order to evaluate the central incisor. The window was made using a metal device with well-formed borders measuring 6 mm in diameter.³ This procedure guaranteed the correct measurement area of interest with reference to shade. In this specific study, the matching area was always the middle one-third of the facial surface of the six anterior teeth. The measurement was performed in all 40 patients by only a single operator using Vita Easyshade (Easyshade, Vident) before the treatment and 30 days after the bleaching therapy. The data obtained by means of the spectrophotometer VITA Easyshade were recorded based on the visual colors of the Vita Classical® color scale (VitaZahnfabrik, Bad Säckingen, Germany). We arranged the shade guide's 16 tabs from highest (B1) to lowest (C4) value, rendering the minimum qualifying shade C1 number 6 (sixth tab on the

value-ordered arrangement). Although this scale is not truly linear, we treated the changes as though they represented a continuous and nearly linear ranking for the purpose of analysis. The color measured at baseline and 30 days after bleaching was used to calculate the variations in color toward the lighter end of the scale (Δ Shade Guide Unit [SGU]).

Study Intervention

After the initial tooth color measurement, orthodontic appliances were bonded to all of the teeth of each patient according to the following technique: commune orthodontic technique white brackets (AVEX MX®, Opal Orthodontics), adhesive, and bonding cement (Transbond™ XT, 3M, St Paul, MN, USA). After this, the bleaching agent was applied for 10 days, with a 45-minute session each day, according to the manufacturer's instructions. In order to properly instruct each participant, the first application of the bleaching agent was performed under professional supervision. After this procedure, the bleaching kits were given to the participants (contents: nine trays of bleaching agent). Ten days after finalization of the treatment, the brackets of the teeth to be evaluated (only in the six anterior teeth) as well as all of the resin cement were removed using aluminum oxide discs (Sof-Lex Pop-on, 3M) in conjunction with a polishing paste (Poligloss, TDV, Pomerode, SC, Brazil). All of these procedures were performed by one orthodontist with more than 20 years of experience in private practice in orthodontia. A new tooth color measurement was performed with the VITA Easyshade spectrophotometer only after 20 days post-bracket removal.

Tooth Sensitivity Evaluation

The patients recorded their perception of tooth sensitivity during the 10 bleaching sessions using three pain scales. A five-point rating scale (0 = none, 1 = mild, 2 = moderate, 3 = considerable, and

Table 2: Absolute Risk of Tooth Sensitivity (%) for the Treatment Groups, with 95% Confidence Interval (CI) for Both Arches*

Groups	Tooth Sensitivity, %	95% CI
TWO	58.8 A	34-74
TWS	73.3 A	53-89

Abbreviations: TWO, Trèswhite Ortho; TWS, Trèswhite Supreme.
* Fisher exact test, p = 0.53.

4 = severe),^{17,18} a 0 to 100 numerical rating scale¹⁹⁻²¹ (NRS 101), and a visual analogue scale¹⁹⁻²¹ using a 10-cm horizontal line with the words “no sensitivity” at one end and the words “highest sensitivity” at the opposite end were used in this study. The highest scores/numerical values obtained in each bleaching session were recorded for statistical purposes. The values were arranged into two categories: percentage of patients who reported tooth sensitivity at least once during treatment (absolute risk of tooth sensitivity) and overall intensity of tooth sensitivity.

Statistical Analysis

The analysis followed the intention-to-treat protocol and involved all participants who were randomly assigned.¹⁶ The statistician was blinded to the study groups. The agreement between examiners’ objective evaluations was evaluated using Kappa statistics. The primary outcome of absolute risk of tooth sensitivity was compared using the Fisher’s exact test at a 5% level of significance. The relative risk as well as the confidence interval for the effect size was calculated.

The intensity of tooth sensitivity (secondary outcome) was also statistically analyzed. The mean/median and standard deviation/interquartile range of the three pain scales were calculated. Color change, another secondary endpoint, was used to assess the effectiveness of the bleaching treatment. To evaluate color change, the means and standard deviations of SGU at baseline and 30 days after

conclusion of bleaching were calculated for each group. In order to evaluate whether the bleaching therapies were effective or not, the data from SGUs of both groups were submitted to the Student *t*-test. In all statistical tests, the significance level was set at $\alpha = 0.05$.

The data sets were plotted on histograms and inspected for normal distributions. Some data did not appear to be normally distributed, and therefore nonparametric statistical tests were used to compare the various treatments. Statistical analyses of three pain scales comparing the two groups at the three different assessment points were performed using the Mann-Whitney *U*-test. In all statistical tests, the significance level was set at $\alpha = 0.05$.

RESULTS

The mean age (years) of the participants in this study was similar between the groups (TWO: 24.4±4.4 years and TWS: 24.2±3.9 years). Fifty-five and 60 percent of the participants in the TWO and TWS groups, respectively, were male. Figure 1 depicts the participant flow diagram in the different phases of the study design. Five patients, two of which were TWO and three of which were TWS, were lost to follow-up because they did not return for the final color evaluation after bracket debonding. However, all patients recorded their perception of tooth sensitivity during the 10 bleaching sessions using three pain scales.

Tooth Sensitivity

The data from 40 patients were used in this study, following the intention-to-treat analysis. With regard to the absolute risk of tooth sensitivity (primary outcome), no significant difference was observed between groups, as seen in Table 2 ($p=0.53$). The absolute risk and 95% confidence interval indicated that there was no difference in tooth sensitivity between the two gels used. With regard to the intensity of tooth sensitivity (Table 3), the groups did

Table 3: Comparison of Tooth Sensitivity Intensity Experienced by Patients of the Treatment Groups, Using Three Pain Scales, at All Evaluation Times*

	0-4**		VAS***		NRS-101***	
	TWO	TWS	TWO	TWS	TWO	TWS
All evaluation times	1 (0/3) A	1 (0/3) A	4.7 ± 8.3 A	8.5 ± 14.5 A	5.1 ± 14.4 A	6.2 ± 12.3 A

Abbreviations: TWO, Trèswhite Ortho; TWS, Trèswhite Supreme; VAS, visual analogue scale; NRS, numerical rating scale.
* Comparisons are valid only within the same pain scale. The two treatments were compared using the Mann-Whitney U-test, and differences are represented by different letters according to the pain scale used; ** Medians (minimum/maximum) values; *** Means and standard deviations.

Table 4: Means and Standard Deviations of Δ Shade Guide Unit (SGU) for the Two Treatment Groups at End of Treatment*

	23	22	21	11	12	13
TWO	7.3 \pm 3.1	8.4 \pm 3.2	9.6 \pm 3.1	9.1 \pm 2.7	8.0 \pm 2.9	7.6 \pm 3.3
TWS	5.3 \pm 3.0	8.0 \pm 2.6	9.5 \pm 2.3	9.3 \pm 3.5	7.2 \pm 3.4	6.2 \pm 3.4

Abbreviations: TWO, Trèswite Ortho; TWS, Trèswite Supreme.
* No statistically significant difference was observed for any tooth evaluated for Δ SGU (Student-t-test, $p > 0.05$).

not differ statistically according to the three pain scales used in this study ($p > 0.05$).

Color Evaluation

Significant whitening was observed in both study groups by the evaluation method used ($p < 0.001$). Whitening of approximately 5 to 9 SGUs was detected for both groups (Table 4). The results of the visual shade guide evaluation matched the hypothesis of equality between the values after bleaching ($p > 0.63$).

DISCUSSION

The results of the present study indicated that both the TWO and TWS groups demonstrated significant tooth color enhancement during orthodontic treatment when compared with baseline. This result is possibly explained by the similarity between the general composition, and especially the concentration, of the bleaching gels (data provided by the manufacturer). This indicates the rejection of the first null hypothesis.

However, the most relevant result was the pattern of bleaching. In our study, we found an average variation of 7.3-9.6 and 5.3-9.5 SGUs for TWO and TWS, respectively, which is in agreement with the results of previous studies.³ These authors clinically tested the effectiveness of 8% hydrogen peroxide (TWO) on bleaching during orthodontic treatment. They showed a mean variation of 4-13 SGUs for TWO after it was used for 10 consecutive days in 45-minute daily sessions.

When studies of at-home bleaching and over-the-counter methods were compared, in which hydrogen peroxide concentrations ranging from 6.5% to 9.5 % were used, the pattern of bleaching of TWO and TWS was similar to that obtained in previous studies,^{11,12,22} which showed a reduction ranging between 4.8 and 9.4 SGUs. However, in the cited studies in general, the time of application comprised a period of at least of two weeks,²² a longer time in comparison with that used in the present study. This bleaching effect may have been strongly influenced by the pH of the gels tested in this study. The pH of

TWO and TWS is 7.3 and 6.7, respectively (data not shown). This high pH level is possibly a result of the addition of sodium hydroxide, which increases the pH of the hydrogen peroxide, contributing to its decomposition.^{23,24}

Most bleaching gels are delivered in acid solutions because they are more stable at a low pH than at higher pH values.²⁵ However, according to the pH of the gel and the pH of the medium, a significant difference was shown between the products released and the kinetics of decomposition of the bleaching gels. Oxygen-free radicals and hydroxyl anions are more frequently produced by the low-pH gels; however, an alkaline solution has a higher concentration of perhydroxyl ions.²⁶ In the case of TWO and TWS, sodium hydroxide is the component responsible for increasing the pH. This strategy has recently been successfully used in the in-office bleaching agents with very good results in terms of bleaching effectiveness associated with lower levels of tooth sensitivity.^{1,17,18}

Some researchers have reported that the hydrogen peroxide formed in an alkaline environment has better bleaching effectiveness,^{24,25,27} attaining up to 50% more bleaching effect.²⁶ Some studies have established that the constant dissociation of hydrogen peroxide could be increased by up to 2.7 times when the peroxide is formed in a pH of 9, when compared with an acid solution of hydrogen peroxide with a pH of 4.4.²⁸

It seems to be surprising that hydrogen peroxide, even when it is not in direct contact with the buccal surface of the teeth, has the ability to bleach them; still, this effect has previously been demonstrated.^{3,4} This is explained by the fact that TWO and TWS present hydrogen peroxide in their compositions. Hydrogen peroxide has the ability to act in a multidirectional manner on dentin; this associated with the fact of its low molecular weight allows hydrogen peroxide diffusion through the enamel porosity to dentin by the formation of free radicals that interact with the pigmented organic molecules, destabilizing and bleaching them, and thus producing the whitening effect.^{9,29}

On the other hand, when hydrogen peroxide is in contact with the tooth structure, protein denaturation occurs, promoting the loss of enamel and dentin matrix substance and increasing porosity, facilitating the permeability of hydrogen peroxide into the pulp chamber, as has been shown in previous studies.^{30,31} This triggers an inflammatory process due to the chemical irritation produced by hydrogen peroxide,³² generating tooth sensitivity during and after the treatment,^{9,33} which is common and reversible for at-home/over-the-counter products.

As mentioned in the Introduction, tooth sensitivity associated with dental bleaching is a common and transitory effect,¹³ and this effect is directly related to the quantity of hydrogen peroxide that diffuses through the tooth structures and depends on the initial concentration of the bleaching agent.^{14,15,34}

The results of the present study indicate that the TWO and TWS groups demonstrated a prevalence of sensitivity of 58.3% and 73.8%, respectively, showing a similar pattern between them and one that is also comparable with that described in the literature when equivalent concentrations are evaluated/used.^{1,10-12} This indicates the rejection of the second null hypothesis.

The percentage difference in sensitivity between the two tested gels could be explained by the difference in concentration of hydrogen peroxide in their composition (TWO: 8% and TWS: 10%), considering that additional factors, such as frequency of application, pH, and others,^{13,30,31} were very similar between them.

Moreover, it is noteworthy that in spite of the high concentration of hydrogen peroxide in the compositions of the two tested gels, both showed a slight low intensity of sensitivity comparable with results in the literature.^{1,11} Suggested hypotheses may contribute to explaining this phenomenon. For example, the phenomenon may be related to the fact that the tray does not remain in direct contact with the tooth structure, either because the tray is not customized, in contrast with at-home products, or because of the interposition of the orthodontic appliance, when compared with treatment performed with at-home and over-the-counter products. During treatment, this could lead to a decrease in the concentration due to likely dilution in saliva, although this fact did not have any influence on the bleaching pattern.

Another factor that could contribute to explaining these findings is the fact that the two products have

desensitizer agents in their composition, in this case, sodium fluoride. It has been demonstrated that products containing desensitizers show a pattern of low sensitivity.^{17,18,35,36}

The high pH of the two tested bleaching agents presented, as previously mentioned, could help to explain these results. The increase in pH due to the presence of sodium hydroxide is responsible for the production of a higher concentration of perhydroxyl ions in comparison with low-pH gels, which more frequently produce hydroxyl anions.²⁶ When gels with higher pH are tested, lower levels of intensity of sensitivity have usually been observed.^{1,17,18} More recently, some articles have shown that the TWS gel has the lowest kinetic rate of hydrogen peroxide release in comparison with different products tested.³⁷ In this study, only around 60%-65% of the hydrogen peroxide concentration was released after 45 minutes of application, in comparison with 80-100% after around 60 minutes of application of the other products tested. The authors' explanation for this slow release is that they modified the matrix composition of the TWS;³⁷ nevertheless, this question deserves attention in future studies.

It is important to mention that five subjects were lost to follow-up because they did not return for final color measurement. The bracket removal and final color measurement were performed in two different appointments to give an adequate time for the teeth to rehydrate after the polishing procedure and before the final color measurement was conducted.³⁸⁻⁴⁰ However, all patients recorded their perception of tooth sensitivity during the 10 bleaching sessions using three pain scales. This is the reason for different numbers of subjects when considering sensitivity evaluation (30 subjects) and color evaluation (25 subjects).

CONCLUSIONS

In conclusion, the results of this study indicate that the use of these new bleaching agents, based on hydrogen peroxide at 8% and 10%, produced bleaching patterns similar to those associated with other types of bleaching agents in patients with fixed orthodontic appliances, in spite of producing a high prevalence of sensitivity, an effect that was transitory and of low intensity.

Acknowledgement

The authors would like to thank Ultradent Dental Products for the donation of the bleaching gel used in this investigation.

Regulatory Statement

This study was conducted in accordance with all the provisions of the local human subjects oversight committee guidelines and policies of: State University of Ponta Grossa. The approval code for this study is: 19033/10.

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, and/or company that is presented in this article.

(Accepted 28 October 2015)

REFERENCES

- Basting RT, Amaral FL, Franca FM, & Florio FM (2012) Clinical comparative study of the effectiveness of and tooth sensitivity to 10% and 20% carbamide peroxide home-use and 35% and 38% hydrogen peroxide in-office bleaching materials containing desensitizing agents *Operative Dentistry* **37(5)** 464-473.
- Kihn PW (2007) Vital tooth whitening *Dental Clinics of North America* **51(2)** 319-331, viii.
- Jadad E, Montoya J, Arana G, Gordillo LA, Palo RM, & Loguercio AD (2011) Spectrophotometric evaluation of color alterations with a new dental bleaching product in patients wearing orthodontic appliances *American Journal of Orthodontics and Dentofacial Orthopedics* **140(1)** 43-47.
- Sundfeld RH, Machado LS, de Oliveira FG, Santos EA, Lugato IC, & Sundfeld Neto D (2012) Conservative reconstruction of the smile by orthodontic, bleaching, and restorative procedures *European Journal of Dentistry* **6(1)** 105-109.
- Zachrisson BU (2005) Incisal edge recontouring in orthodontic finishing *World Journal of Orthodontics* **6(4)** 398-405.
- Polo M (2005) Botulinum toxin type A in the treatment of excessive gingival display *American Journal of Orthodontics and Dentofacial Orthopedics* **127(2)** 214-218.
- Sarver DM, & Yanosky M (2005) Principles of cosmetic dentistry in orthodontics: Part 2. Soft tissue laser technology and cosmetic gingival contouring *American Journal of Orthodontics and Dentofacial Orthopedics* **127(1)** 85-90.
- Thickett E, & Cobourne MT (2009) New developments in tooth whitening. The current status of external bleaching in orthodontics *Journal of Orthodontics* **36(3)** 194-201.
- Haywood VB, & Heymann HO (1991) Nightguard vital bleaching: How safe is it? *Quintessence International* **22(7)** 515-523.
- Donly KJ, Sequra A, Sasa I, Perez E, Anastasia MK, & Farrell S (2010) A controlled clinical trial to evaluate the safety and whitening efficacy of a 9.5% hydrogen peroxide high-adhesion whitening strip in a teen population *American Journal of Dentistry* **23(5)** 292-296.
- Ontiveros JC, Eldiwany MS, & Paravina R (2012) Clinical effectiveness and sensitivity with overnight use of 22% carbamide peroxide gel *Journal of Dentistry* **40(2)** 17-24.
- Alonso de la Peña V, & López Ratón M (2014) Randomized clinical trial on the efficacy and safety of four professional at-home tooth whitening gels *Operative Dentistry* **39(2)** 136-143.
- Haywood VB (2005) Treating sensitivity during tooth whitening *Compendium of Continuing Education in Dentistry* **26(9 Supplement 3)** 11-20.
- Benetti A, Valera M, Mancini M, Miranda C, & Balducci I (2004) In vitro penetration of bleaching agents into the pulp chamber *International Endodontic Journal* **37(2)** 120-124.
- Hanks C, Fat J, Wataha J, & Corcoran J (1993) Cytotoxicity and dentin permeability of carbamide peroxide and hydrogen peroxide vital bleaching materials in vitro *Journal of Dental Research* **72(5)** 931-938.
- Schulz KF, Altman DG, & Moher D (2010) CONSORT 2010 statement: Updated guidelines for reporting parallel group randomised trials *Journal of Pharmacology and Pharmacotherapeutics* **1(2)** 100-107.
- Kossatz S, Martins G, Loguercio AD, & Reis A (2012) Tooth sensitivity and bleaching effectiveness associated with use of a calcium-containing in-office bleaching gel *Journal of the American Dental Association* **143(12)** e81-e87.
- Reis A, Kossatz S, Martins GC, & Loguercio AD (2013) Efficacy of and effect on tooth sensitivity of in-office bleaching gel concentrations: A randomized clinical trial *Operative Dentistry* **38(4)** 386-393.
- Jensen MP, Karoly P, & Braver S (1986) The measurement of clinical pain intensity: A comparison of six methods *Pain* **27(1)** 117-126.
- Caraceni A, Cherny N, Fainsinger R, Kaasa S, Poulain P, Radbruch L, & De Conno F (2002) Pain measurement tools and methods in clinical research in palliative care *Journal of Pain and Symptom Management* **23(3)** 239-255.
- Noble B, Clark D, Meldrum M, ten Have H, Seymour J, Winslow M, & Paz S (2005) The measurement of pain, 1945-2000 *Journal of Pain and Symptom Management* **29(1)** 14-21.
- Alonso de la Peña V, & Balboa Cabrita O (2006) Comparison of the clinical efficacy and safety of carbamide peroxide and hydrogen peroxide in at-home bleaching gels *Quintessence International* **37(7)** 551-556.
- Marshall MV, Gragg PP, Packman EW, Wright PB, & Cancro LP (2001) Hydrogen peroxide decomposition in the oral cavity *American Journal of Dentistry* **14(1)** 39-45.
- Zantner C, Derdilopoulou F, Martus P, & Kielbassa AM (2006) Randomized clinical trial on the efficacy of 2 over-the-counter whitening systems *Quintessence International* **37(9)** 695-706.
- Chen JH, Xu JW, & Shing CX (1993) Decomposition rate of hydrogen-peroxide bleaching agents under various chemical and physical conditions *Journal of Prosthetic Dentistry* **69(1)** 46-48.
- Sun G (2000) The role of lasers in cosmetic dentistry *Dental Clinics of North America* **44(4)** 831-850.

27. Trotman ER (1985) *Dyeing and Chemical Technology of Textile Fibres* **6th edition** John Wiley and Sons, New York, NY.
28. Frysh H, Bowles WH, Baker F, Rivera-Hidalgo F, & Guillen G (1995) Effect of pH on hydrogen peroxide bleaching agents *International Journal of Esthetic Dentistry* **7(3)** 130-133.
29. Joiner A (2006) The bleaching of teeth: A review of the literature *Journal of Dentistry* **34(7)** 412-419.
30. Joiner A (2007) Review of the effects of peroxide on enamel and dentine properties *Journal of Dentistry* **35(12)** 889-896.
31. Attin T, Schmidlin PR, Wegehaupt F, & Wiegand A (2009) Influence of study design on the impact of bleaching agents on dental enamel microhardness: A review *Dental Materials* **25(2)** 143-157.
32. Haywood VB (2000) Current status of night guard vital bleaching *Compendium of Continuing Education in Dentistry* **28(48)** 10-17.
33. Nathanson D (1997) Vital tooth bleaching: Sensitivity and pulpal considerations *Journal of the American Dental Association* **128(Supplement)** 41S-44S.
34. Sulieman M, MacDonald E, Rees JS, Newcombe RG, & Addy M (2006) Tooth bleaching by different concentrations of carbamide peroxide and hydrogen peroxide whitening strips: An in vitro study *Journal of Esthetic and Restorative Dentistry* **18(2)** 93-100.
35. Browning WD, Chan DC, Myers ML, Brackett WW, Brackett MG, & Pashley DH (2008) Comparison of traditional and low sensitivity whiteners *Operative Dentistry* **33(4)** 379-385.
36. Matis BA, Cochran MA, Eckert GJ, & Matis JI (2007) In vivo study of two carbamide peroxide gels with different desensitizing agents *Operative Dentistry* **32(6)** 549-555.
37. da Silva Marques DN, Silveira JM, Marques JR, Amaral JA, Guilherme NM, & da Mata AD (2012) Kinetic release of hydrogen peroxide from different whitening products *European Journal of Esthetic Dentistry* **7(3)** 344-352.
38. Russell MD, Gulfranz M, & Moss BW (2000) In vivo measurement of colour changes in natural teeth *Journal of Oral Rehabilitation* **27(9)** 786-792.
39. Du RX, Li YM, & Ma JF (2012) Effect of dehydration time on tooth colour measurement in vitro *Chinese Journal of Dental Research* **15(1)** 37-39.
40. Burki Z, Watkins S, Wilson R, & Fenlon M (2013) A randomised controlled trial to investigate the effects of dehydration on tooth colour *Journal of Dentistry* **41(3)** 250-257.