Low Concentration H_2O_2/TiO_N in Office Bleaching: A Randomized Clinical Trial

J.F. Bortolatto, H. Pretel, M.C. Floros, A.C.C. Luizzi, A.A.R. Dantas, E. Fernandez, G. Moncada and O.B. de Oliveira, Jr.

J DENT RES 2014 93: 66S originally published online 27 May 2014
DOI: 10.1177/0022034514537466

CLINICAL TRIALS

Low Concentration H_2O_2/TiO_N in Office Bleaching: A Randomized Clinical Trial

J.F. Bortolatto[1]*, H. Pretel[2], M.C. Floros[3], A.C.C. Luizzi[1], A.A.R. Dantas[1], E. Fernandez[4], G. Moncada[4], and O.B. de Oliveira Jr.[1]

Abstract: ***Objectives:*** *The purpose of this randomized double-blinded clinical trial was to test the efficacy and tooth sensitivity promoted by the use of an in-office 15% H_2O_2 bleaching agent containing nanoparticles of TiO_N photocatalyzed with LED/laser light (HP15) and a control of 35% H_2O_2 (HP35).* ***Methods:*** *Forty healthy volunteers, both sexes, aged 18 to 25 yr, were randomly distributed in 2 groups: HP15 (n = 20) was treated in 3 sessions of 48 min each, and HP35 (n = 20) was treated in 3 sessions of 45 min each. The efficacy (E) was evaluated by ΔE values measured via reflectance spectroscopy. The tooth sensitivity (S) was analyzed by visual analog scale (low, average, high, very high). The absolute risk reduction and the number needed to treat index were calculated. The data were analyzed by mixed repeated measures analysis of variance with Bonferroni-correction t test (α = 0.05).* ***Results:*** *For the efficacy, significant differences were found for number of bleaching sessions (p = .0001; η_p^2 = 0.73 and π = 1.000) and for the interaction of number of sessions and bleaching protocols (p = .0001; η_p^2 = 0.319 and π = 1.000. The tooth sensitivity level showed significant differences only between the bleaching protocols. Absolute risk reduction calculated was 52% and number needed to treat, 1.92.* ***Conclusions:*** *The bleaching agent with the lower concentration (HP15) promoted lower levels of tooth sensitivity and presented greater efficacy compared to the control (HP35) in patients between 18 and 25 yr old. The limitation of short-term evaluation did not provide information about the longevity of the tooth bleaching (Brazilian Clinical Trials Registry Re Bec no. U1111-1150-4466).*

Key Words: tooth bleaching, hydrogen peroxide, nanotechnology, titanium dioxide, dentin sensitivity, clinical protocols.

Introduction

Tooth bleaching is the most frequently requested procedure by patients because it is considered a highly effective, minimally invasive, biologically safe treatment for discolored teeth. However, there is still much controversy in relation to the protocols and the safety of the techniques (Dahl and Pallesen, 2003).

In-office tooth bleaching is traditionally performed with high concentrations of hydrogen peroxide (35% to 38%), a chemical substance that possesses a high oxidative power (Joiner, 2006; Buchalla and Attin, 2007). It can dissociate into water, oxygen, and some species of free radicals. These radicals can degrade complex organic molecules, reducing or altering the compounds by redox reactions (Kwon *et al.*, 2002; Kawamoto and Tsujimoto, 2004; Tredwin *et al.*, 2006). Although bleaching has aesthetic benefits, the free radicals are potentially damaging to biological tissues (Wee *et al.*, 2002; Dahl and Pallesen, 2003; Costa *et al.*, 2010) because of their high oxidative power.

The major side effect of tooth bleaching is tooth sensitivity during and after the treatment, which represents the degree of biological damage of tooth bleaching (Costa *et al.*, 2010; Kossatz *et al.*, 2011; Martin *et al.*, 2013). Several studies show that the indirect cytotoxicity of the free radicals is proportional to the concentration of the bleaching agent as well as the contact time with the enamel (Kwon *et al.*, 2002; Kawamoto and Tsujimoto, 2004; Tredwin *et al.*, 2006). A study by Costa *et al.* (2010) found that the bleaching agent caused irreversible pulp damage in the lower incisors when in high concentrations and when in contact with the tooth for 45 min.

DOI: 10.1177/0022034514537466. [1]Department of Restorative Dentistry, Araraquara School of Dentistry, UNESP, Univ Estadual Paulista, Brazil; [2]NUPEN, Resea; [3]Trent Center for Biomaterials Research, Departments of Physics and Astronomy and Chemistry, Trent University, Canada; and [4]School of Dentistry of Santiago, Universidad de Chile, Chile; *corresponding author, janainabortolatto@hotmail.com

A supplemental appendix to this article is published electronically only at http://jdr.sagepub.com/supplemental.

Bleaching agents with low hydrogen peroxide concentration have recently been introduced for in-office tooth bleaching, with the claim of increased safety and efficacy over conventional formulations. These products use heterogeneous advanced oxidative processes (POAHe) to produce free radicals. The agent's activity is catalyzed and potentiated by a semiconductor agent—normally, titanium dioxide, which is activated by light sources. According to Maetani *et al.* (2008) and Suemori *et al.* (2008), the new generation of bleaching agents is safer and more effective and promotes the bleaching processes without the presence of the hydroxyl radical, thereby minimizing dental structure damage. However, a study by Sakai *et al.* (2007) found the opposite. They proposed that POAHe results in a greater rate of formation of reactive radicals than were obtained in the homogeneous process. Martin *et al.* (2013) compared the dentin hypersensitivity after 3 different bleaching protocols. They found that, in contrast to 35% of hydrogen peroxide, the new generation of 15% hydrogen peroxide bleaching agents presented the lowest change of sensitivity in relation to baseline.

This study investigated the efficacy and tooth sensitivity caused by an in-office 15% H_2O_2 bleaching agent containing nanoparticles of TiO_N and the control 35% H_2O_2 to test the null hypothesis that HP15 containing nanoparticles of TiO_N presents similar efficacy and tooth sensitivity compared to HP35.

Materials & Methods

This randomized clinical trial was approved by the Ethics Committee of the Araraquara Dental School (UNESP, Brazil; protocol no. 51/08) and took place at this location. It is registered in the Brazilian Clinical Trials Registry (ReBec no. U1111-1150-4466), where the full trial protocol can be accessed.

Between 2010 and 2011, 66 volunteers were examined in a dental chair to check if they met the inclusion and exclusion criteria. Forty volunteers between 18 and 25 yr old were selected for the study under the following inclusion criteria: anterior healthy teeth without restorations, bleaching experience, cervical lesions, or dental pain and with properly aligned teeth. Exclusion criteria were as follows: pregnancy or breastfeeding, a maximum of TF3 fluorosis, tetracycline stains, orthodontic treatment, periodontal disease, orofacial tumors, trauma, tooth malformation, or anti-inflammatory drug intake.

Patients were referred by the university clinic. Two trained operators performed the bleaching treatments. Each patient's bleaching protocol group was assigned by simple draw, with a box and pieces of paper, each containing the name of a protocol. When the patient came for the first appointment, the operator drew a piece of paper and applied the respective treatment. The operators were allocated to each group randomly; both were calibrated to work with the 2 bleaching agents: a 15% H_2O_2 agent containing TiO_N nanoparticles (HP15; experimental) and a 35% H_2O_2 agent (HP35; positive control). Patients and examiners were both blinded to the bleaching protocol used.

Sample Size Calculation

Data used to calculate the minimum sample size were obtained from a pilot study. They were calculated with the software G*Power 3.1.7 according to the repeated measurements design, in which the treatment was considered the independent factor and the application times as the repeated measures factor. With a significant level of 5%, statistic power of 80%, and effect size of 21%, the sample size was calculated as 16 participants for each group. A total of 20 participants were used to compensate an estimated 20% dropout rate.

Experimental Protocol

The 40 volunteers selected were encoded and randomly distributed into 2 groups (n = 20). They received a dental prophylaxis and oral hygiene instructions 1 wk before the beginning of this study to create similar initial oral conditions. They also signed a term of free and informed consent. The maxillary anterior teeth shade was measured with a Vita Easyshade® (Vident, Brea, CA, USA) spectrophotometer prior to the bleaching treatment (T0; baseline).

In each session, volunteers received prophylaxis with pumice powder and water. Then, the gum barrier was adequately applied and photopolymerized with LED/laser light (Whitening Lase II, DMC, São Carlos, Brazil) consisting of 6 LEDs (470 ± 15 nm/ blue light), generators of 1800 mW of power, and 3 low-intensity lasers (808 nm/ infrared light), generators of 600 mW of power, irradiating a total area of 8.5 cm^2, with an intensity of 300 mW/cm^2.

The bleaching agents were prepared by mixing the "peroxide" and "thickening" compounds, according to the manufacturer's instructions. The resultant gel was distributed uniformly on the buccal surfaces of the upper and lower teeth. A total of 16 teeth, between the first premolars, were bleached for each patient with the application of 24 peroxide drops and 8 thickening drops.

In HP15 (Lase Peroxide Lite, DMC, São Carlos, Brazil), the bleaching gel was applied in 3 sessions of 48-min duration, divided into 3 applications of 16 min. The gel was photocatalyzed 4 times for each arcade, with alternating irradiance every 2 min, via a hybrid light (LED/laser; Whitening Lase II). The total photocatalyzation time over 3 bleaching sessions was 144 min.

In the control group (HP35; Lase Peroxide Sensy, DMC, São Carlos, SP, Brazil), the bleaching gel was applied in 3 sessions of 45-min duration, divided into 3 applications of 15 min without photocatalyzation. The total bleaching time over 3 bleaching sessions was 135 min.

The intervals of applications were 7 d between appointments for both groups.

Efficacy Evaluation (E)

A blinded evaluator measured the tooth color for the baseline (T0) and immediately after first, second, and third appointments (T1, T2, T3). The reflectance spectrophotometer Vita EasyShade was calibrated and positioned in the middle third of the labial

surface, following the manufacturer's instructions. The shade was determined via the parameters of L*, a*, and b* obtained, and the color alteration after each application time was given by the differences between the 2 colors (ΔE), calculated per the following formula: $\Delta E=\sqrt{(\Delta L)^2+(\Delta a)^2+(\Delta b)^2}$ (Mokhlis *et al.*, 2000).

Tooth Sensitivity Evaluation

Tooth sensitivity (S) was measured with a visual analog scale. Patients quantify their sensitivity, marking a 100-mm line anchored between 0 mm ("no pain") at the left side and 100 mm ("very severe pain") at the right end (Holland *et al.*, 1997). The visual analog scale analysis was carried out 4 times (T0, T1, T2, T3).

The number of patients reporting tooth sensitivity, without considering the level of sensitivity, was used to calculate the absolute risk reduction (ARR) and the number needed to treat (NNT). The ARR and the NNT were calculated by equations 1 and 2:

$$ARR = CSR - ESR \quad (1)$$

$$NNT = 1 / (CSR - ESR), \quad (2)$$

where CSR = control sensitivity rate and ESR = experimental sensitivity rate.

Statistical Analysis

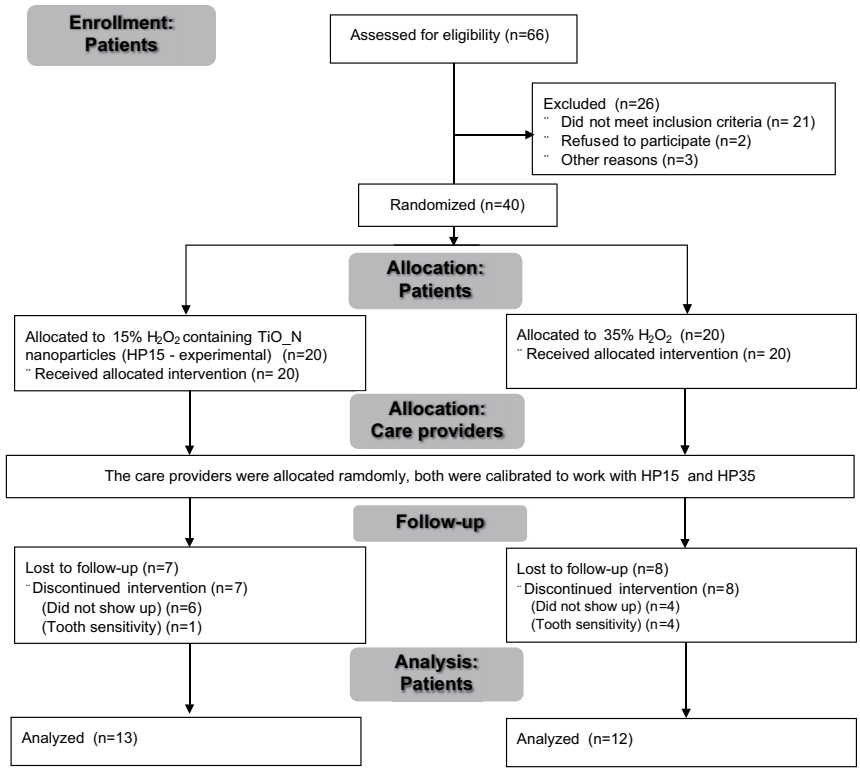
After the normality of the data distribution and the homogeneity of variances were verified, efficacy of the treatments were evaluated over total alteration of color (ΔE) and tooth sensitivity reported by the patients. Both were analyzed by a mixed repeated measures analysis of variance test, with groups and application times as independent factors.

In all tests, the significance was set at 5%, and calculations were performed with SPSS 19.0.

Results

The mean age of the participants starting this study was similar (HP15: 20.7 ± 2.4 yr; HP35: 21.5 ± 2.1 yr); 20% and 5% of the participants of HP15 and HP35, respectively, were men. Twenty-five completed the treatment (62.5%); 7 (all women) dropped out from group HP35 and 8 (1 man and 7 women) from group HP15. The dropouts (after the first or second appointment) were due to patients who could not be contacted, who did not explain their reason, or who had tooth sensitivity. Although the dropout rate was higher than that estimated in the pilot study, the observed power of the analysis was not affected (Appendix Tables 1 and 3). The Figure shows the participants' flow diagram in different phases of the study design.

Figure.
CONSORT flow diagram detailing the recruitment and enrollment of the clinical trial.



Efficacy (E)

The analysis of variance test demonstrated significant differences for the application time (p = .0001) and for the interaction of application time and groups (p = .0001). These results prove that bleaching efficacy varies according to the number of sessions realized and that the bleaching protocols had a significant influence on the bleaching efficacy (p = .05). This difference has a very high effect size and test power (η_p^2 = 0.73 and π = 1.000; Appendix Table 1).

The mean of efficacy (ΔE), the standard deviation, and the 95% confidence interval for groups and application times are described in Table 1, which shows that the efficacy of the lower-concentration bleaching protocol is greater than the traditional treatment (HP35). Differences in ΔL, Δa, and Δb can be seen in Appendix Table 2.

Tooth Sensitivity (S)

No significant difference in tooth sensitivity reported between the application times was shown. In contrast, both groups demonstrated different levels of tooth sensitivity (p = .004). This difference has a very high effect size and statistic power (η_p^2 = 0.30 and π = 0.86; Appendix Table 3).

The mean of tooth sensitivity (S) reported by the volunteers, the standard deviation, and 95% confidence interval

Table 1.
Efficacy for Groups and Application Times

Protocols	Efficacy (ΔE)					
	T1		T2		T3	
	Mean ± SD	95% CI	Mean ± SD	95% CI	Mean ± SD	95% CI
HP15L (*n* = 12)	2.38 ± 1.26	1.58, 3.18	6.94 ± 1.83	5.77, 8.10	8.92 ± 2.36	7.43, 10.42
HP35 (*n* = 13)	3.35 ± 2.09	2.09, 4.61	5.12 ± 1.40	4.27, 5.97	6.66 ± 2.73	4.77, 7.39

SD, standard deviation; CI, confidence interval.

Table 2.
Tooth Sensitivity Reported for Groups and Application Times

Protocols	Tooth Sensitivity (%)					
	T1		T2		T3	
	Mean ± SD	95% CI	Mean ± SD	95% CI	Mean ± SD	95% CI
HP15L (*n* = 12)	0.50 ± 1.7	–0.60, 1.60	3.75 ± 9.30	–2.17, 9.57	11.67 ± 24.80	–4.09, 27.43
HP35 (*n* = 13)	30.08 ± 26.00	14.39, 45.77	20.77 ± 22.70	7.04, 34.50	35.46 ± 35.8	13.83, 57.09

SD, standard deviation; CI, confidence interval.

Table 3.
Patients Reporting Tooth Sensitivity

Treatment	Patients Reporting Sensitivity, *n*		Sensitivity Rate, %	Absolute Risk Reduction, %	No. Needed to Treat
	Yes	No			
HP15, experimental	4	9	31	52	1.92
HP35, control	10	2	83		

for groups and application times are described in Table 2. There is a significant difference between the 2 groups. The ARR and the NNT calculated were 52% and 1.92, respectively (Table 3).

Discussion

In this study, the null hypothesis proposed has been rejected, showing that 15% H_2O_2 gel containing nanoparticles of TiO_N is greater in its efficacy compared with the traditional treatment while providing a lower occurrence of tooth sensitivity.

It was previously thought that to obtain the greatest effectiveness of whitening, the highest concentration of bleaching gel should be applied for the longest contact time with the tooth structure (Heymann, 2005). However, this practice focuses on obtaining the best aesthetic results, without considering the undesirable side effects (Fugaro *et al.*, 2004; Leonard *et al.*, 2007).

In an attempt to combine efficacy and safety, new bleaching agents with lower concentrations of hydrogen peroxide have been introduced to the market based on the catalytic action of a nanoparticle semiconductor additive (Arens *et al.*, 1972; Sakai *et al.*, 2007; Suemori *et al.*, 2008). The heterogeneous advanced oxidative process bases its action on semiconductor chemical agents that, when exposed to solar light or artificial ultraviolet light, catalyze the formation of hydroxyl radicals from hydrogen peroxide. The dependence on ultraviolet radiation for the efficacy of the bleaching agent is one disadvantage of this formulation because of its potentially harmful effects (Brenneisen *et al.*, 2002; Labrie *et al.*, 2011). In this new formulation, titanium oxide nanoparticles doped with nitrogen enables the catalytic activity to occur when exposed to wavelengths in the band of the visible light, avoiding the use of ultraviolet light (Sulieman *et al.*, 2003; Suemori *et al.*, 2008).

According to Sakai *et al.* (2007), the incorporation of the TiO_N nanoparticles in hydrogen peroxide allows a reduction in the concentration required of the latter, improving the biocompatibility of the final product and thereby preventing postoperative sensitivity and increasing the safety of the bleaching processes. The irradiation with an appropriate light source will generate high concentrations of free radicals and other reactive species of oxygen necessary for breaking the molecular bonds of pigments within the dental structure. The gel used in this study is composed of this new formulation that improves its reactivity when exposed to a simultaneous LED/laser light.

The results showed greater efficacy when the bleaching agent with 15%

hydrogen peroxide with TIO_N nanoparticles was used, given the contact time and reduced concentration for HP15. These results are according to Matis *et al.* (2007), in which the contact time can be important but the concentration was not a relevant factor. There is a significant influence for both the concentration group and the application time. The greater efficacy of the lower-concentration bleaching protocol is not clear in the first session (T1), but it is shown on the following sessions and demonstrates the efficacy of the protocol using LED/laser light and the POAHe modulated by TIO_N nanoparticles. The absence of long-term measurements is a limitation of this study and does not provide information on the longevity of the treatments.

Regarding tooth sensitivity, even though no statistically significant difference was found between the bleaching sessions, there is a significant difference between the 2 groups. Table 2 shows that the level of tooth sensitivity caused by HP15 can be classified as low sensitivity, while the sensitivity caused by HP35 is significantly higher. This result can be attributed to the reduced concentration of hydrogen peroxide, the photocatalyzation by LED/laser light (Kishi *et al.*, 2011; Bortolatto *et al.*, 2013), or the interaction between the 2 factors. These results agree with Maetani *et al.* (2008), who showed that formulations with reduced hydrogen peroxide concentrations containing TiO_2 can be similar or more effective than traditional 35% hydrogen peroxide concentrations, with the advantage of greater safety and less risk of tooth sensitivity. A study by Suemori *et al.* (2008) demonstrated the effectiveness of heterogeneous photocatalysis mediated by TiO_2. The findings of Moncada *et al.* (2013), Benetti *et al.* (2004), Gökay *et al.* (2004), and Martin *et al.* (2013) also showed that increasing peroxide concentrations would increase tooth sensitivity. The absence of long-term measurements in this study limited the evaluation of side effects over time. However, studies using the same bleaching agents demonstrate that sensitivity returned to normal within a week (Mondelli *et al.*, 2012; Martin *et al.*, 2013; Moncada *et al.*, 2013).

The ARR is the difference in the probabilities of an event in the control and experimental groups. In this study, the ARR calculated was 52%, which means that the probability of tooth sensitivity rate in the experimental group is significantly lower than that in the control. If the event rate in the experimental group is less than that in the control group, this suggests a potential benefit from the new treatment. The NNT can be expressed as the reciprocal of the ARR. The reciprocal of 52% is 1.92, implying that a dentist would need to treat, on average, 1.92 patients to expect to prevent 1 tooth sensitivity report (Cook and Sackett, 1995).

Conclusion

The use of HP15 containing TiO_N photocatalyzed with LED/laser light in patients between 18 and 25 yr old results in lower tooth sensitivity compared to a conventional 35% H_2O_2 and provides a greater efficacy, suggesting that agents with low concentrations should be the first choice in the interest of patient safety.

The limitation of short-term evaluation did not provide information about the longevity of the tooth bleaching.

Acknowledgments

This study was supported by CAPES and FAPESP protocol no. 2010/08873-5. We thank NUPEN for the technical and scientific support. The author(s) received no financial support and declare no potential conflicts of interest with respect to the authorship and/or publication of this article.

References

Arens DE, Rich JJ, Healey HJ (1972). A practical method of bleaching tetracycline-stained teeth. *Oral Surg Oral Med Oral Pathol* 34:812-817.

Benetti AR, Valera M, Mancini M, Miranda C, Balducci I (2004). In vitro penetration of bleaching agents into the pulp chamber. *Int Endod J* 37:120-124.

Bortolatto JF, Pretel H, Neto CS, Andrade MF, Moncada G, Junior OBO (2013). Effects of LED-laser hybrid light on bleaching effectiveness and tooth sensitivity: a randomized clinical study. *Laser Phys Lett* 10:085601.

Brenneisen P, Sies H, Scharffetter-Kochanek K (2002). Ultraviolet-B irradiation and matrix metalloproteinases. *Ann N Y Acad Sci* 973:31-43.

Buchalla W, Attin T (2007). External bleaching therapy with activation by heat, light or laser—a systematic review. *Dent Mater* 23:586-596.

Cook RJ, Sackett DL (1995). The number needed to treat: a clinically useful measure of treatment effect. *BMJ* 310:452-454. (Published erratum in: *BMJ* 310:1056, 1995).

Costa CA, Riehl H, Kina JF, Sacono NT, Hebling J (2010). Human pulp responses to in-office tooth bleaching. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 109:e59-e64.

Dahl J, Pallesen U (2003). Tooth bleaching—a critical review of the biological aspects. *Crit Rev Oral Biol Med* 14:292-304.

Fugaro JO, Nordahl I, Fugaro OJ, Matis BA, Mjor I (2004). Pulp reaction to vital bleaching. *Oper Dent* 29:363-368.

Gökay O, Müjdeci A, Algn E (2004). Peroxide penetration into the pulp from whitening strips. *J Endod* 30:887-889.

Heymann H (2005). Tooth whitening: facts and fallacies. *Br Dent J* 198:514.

Holland G, Narhi M, Addy M, Gangarosa L, Orchardson R (1997). Guidelines for the design and conduct of clinical trials on dentine hypersensitivity. *J Clin Periodontol* 24:808-813.

Joiner A (2006). The bleaching of teeth: a review of the literature. *J Dent* 34:412-419.

Kawamoto K, Tsujimoto Y (2004). Effects of the hydroxyl radical and hydrogen peroxide on tooth bleaching. *J Endod* 30:45-50.

Kishi A, Otsuki M, Sadr A, Ikeda M, Tagami J (2011). Effect of light units on tooth bleaching with visible-light activating titanium dioxide photocatalyst. *Dent Mater J* 30:723-729.

Kossatz S, Dalanhol AP, Cunha T, Loguercio A, Reis A (2011). Effect of light activation on tooth sensitivity after in-office bleaching. *Oper Dent* 36:251-257.

Kwon Y, Huo M, Kim K, Kim S, Kim Y (2002). Effects of hydrogen peroxide on the light reflectance and morphology of bovine enamel. *J Oral Rehabil* 29:473-477.

Labrie D, Moe J, Price R, Young ME, Felix CM (2011). Evaluation of ocular hazards from 4 types of curing lights. *J Can Dent Assoc* 77:b116.

Leonard RH, Smith LR, Garland GE, Tiwana KK, Zaidel LA, Pugh G, *et al.* (2007). Evaluation

of side effects and patients' perceptions during tooth bleaching. *J Esthet Restor Dent* 19:355-364.

Maetani T, Yoshida F, Yoshida A, Sugiyama S, Nishimura T, Tani-Ishii N, *et al.* (2008). An investigation of application of novel tooth bleaching using low concentration of hydrogen peroxide: dental application of electron spin resonance (ESR) technique for detecting reactive oxygen specie. *Oral Ther Pharmacol* 27:109-115.

Martin J, Fernandez E, Bahamondes V, Werner A, Elphick K, Oliveira OB Jr, *et al.* (2013). Dentin hypersensitivity after teeth bleaching with in-office systems: randomized clinical trial. *Am J Dent* 26:10-14.

Matis B, Cochran M, Franco M, Al-Ammar W, Eckert G, Stropes M (2007). Eight in-office tooth whitening systems evaluated in vivo: a pilot study. *Oper Dent* 32:322-327.

Mokhlis GR, Matis BA, Cochran MA, Eckert GJ (2000). A clinical evaluation of carbamide peroxide and hydrogen peroxide whitening agents during daytime use. *J Am Dent Assoc* 131:1269-1277.

Moncada G, Sepúlveda D, Elphick K, Contente M, Estay J, Bahamondes V, *et al.* (2013). Effects of light activation, agent concentration, and tooth thickness on dental sensitivity after bleaching. *Oper Dent* 38:467-476.

Mondelli RF, Azevedo JF, Francisconi AC, Almeida CM, Ishikiriama SK (2012). Comparative clinical study of the effectiveness of different dental bleaching methods-two year follow-up. *J Appl Oral Sci* 20:435-443.

Sakai K, Kato J, Nakazawa T, Hirai Y (2007). The amounts of hydrogxyl radical generated by titanium dioxide and 3,5% hydrogen peroxide under 405-nm diode laser irradiation. *Laser Phys* 17:1062-1066.

Suemori T, Kato J, Nakazawa T, Akashi G, Igarashi A, Hirai Y, *et al.* (2008). Effects of light irradiation on bleaching by a 3.5% hydrogen peroxide solution containing titanium dioxide. *Laser Phys Lett* 5:379-383.

Sulieman M, Addy M, Rees JS (2003). Development and evaluation of a method in vitro to study the effectiveness of tooth bleaching. *J Dent* 31:415-422.

Tredwin C, Naik S, Lewis N, Scully C (2006). Hydrogen peroxide tooth-whitening (bleaching) products: review of adverse effects and safety issues. *Br Dent J* 200:371-376.

Wee AG, Monaghan P, Johnston WM (2002). Variation in color between intended matched shade and fabricated shade of dental porcelain. *J Prosthet Dent* 87:657-666.