Effectiveness of and tooth sensitivity with at-home bleaching in smokers

A multicenter clinical trial

Juliana Larocca de Geus, DDS, MS; Cristian Bersezio, DDS; Javiera Urrutia, DDS; Toshiro Yamada, DDS; Eduardo Fernández, DDS, PhD; Alessandro Dourado Loguercio, DDS, MS, PhD; Alessandra Reis, DDS, PhD; Stella Kossatz, DDS, MS, PhD

ABSTRACT

Background. The authors conducted a 2-center controlled clinical study to show the equivalence of at-home bleaching in smokers and nonsmokers at 1 week and 1 month and evaluate tooth sensitivity (TS).

Methods. The authors selected 60 smokers and 60 nonsmokers with central incisors of shade A2 or darker. The participants performed bleaching with 10% carbamide peroxide for 3 hours daily for 3 weeks. The authors evaluated the color by using a shade guide and a spectrophotometer before, during, and after bleaching (1 week and 1 month). Patients recorded TS by using a 0-4 scale and a visual analog scale. The authors used multivariable regression analysis to test factors associated with color change and TS ($\alpha = .05$).

Results. Smokers and nonsmokers showed significant color change statistically equivalent to within $\pm$ 2.0 units at 1 week after bleaching. Overall, color shade improved by 4.1 shade guide units (95% confidence interval [CI], 3.7-4.5) and 7.8 units of color change measured with the spectrophotometer (95% CI, 7.1-8.5) at 1 month. None of the factors affected the TS risk. TS absolute risk and intensity were similar between groups ($P > .05$), with an overall estimate of 47% (95% CI, 38-56%).

Conclusions. The immediate effectiveness of whitening- and bleaching-related TS were not affected by smoking.

Practical Implications. Smoking did not affect the immediate color change (1 week). Effective whitening was achieved regardless of whether the patient was a smoker. However, this equivalence was not apparent 1 month after bleaching, with smokers having slightly darker teeth.

Key Words. Tooth bleaching; smoking; dentin sensitivity.

JADA 2015:146(4):233-240. ClinicalTrials.gov identifier NCT02017873.

http://dx.doi.org/10.1016/j.adaj.2014.12.014

Public demand for aesthetic dentistry, including dental bleaching, has increased in recent years.[1] Results from several clinical studies have reported the effectiveness of at-home bleaching with 10% carbamide peroxide (CP).[2-6]

Despite the effectiveness of dental bleaching, tooth sensitivity (TS) is a common adverse effect,[7] which occurs in 37%-90% of patients, even with use of low-concentrate, at-home bleaching gels.[4,6,8-13] In the literature, investigators have reported other detrimental effects

Dr. de Geus is a graduate student, Department of Restorative Dentistry, State University of Ponta Grossa, Paraná, Brazil.
Dr. Bersezio is a graduate student, Department of Restorative Dentistry, University of Chile, Santiago, Chile.
Dr. Urrutia is a graduate student, Department of Restorative Dentistry, University of Chile, Santiago, Chile.
Dr. Yamada is a graduate student, Department of Restorative Dentistry, University of Chile, Santiago, Chile.
Dr. Fernández is an assistant professor, Department of Restorative Dentistry, University of Chile, Santiago, Chile.
Dr. Loguercio is an adjunct professor, Department of Restorative Dentistry, State University of Ponta Grossa, Paraná, Brazil.
Dr. Reis is an adjunct professor, Department of Restorative Dentistry, State University of Ponta Grossa, Paraná, Brazil. Address correspondence to Dr. Reis at Universidade Estadual de Ponta Grossa, Rua Carlos Cavalcanti, 4748, Bloco M, Sala 64A - Uvaranas, Ponta Grossa, Paraná, 84030-900, Brazil, e-mail reis_ale@hotmail.com.
Dr. Kossatz is an associate professor, Department of Restorative Dentistry, State University of Ponta Grossa, Paraná, Brazil.

of bleaching on the enamel surface,[14-16] as well as increased enamel permeability.[17]

These difficulties are probably why professionals usually request that their patients avoid smoking during the bleaching treatment or even refuse this procedure to smokers. Cigarette smoke contains water, air, carbon monoxide, carbon dioxide, and tar. During burning, cigarette components such as tar, sugar, and cocoa are transferred to the smoke.[18] These components cause dental discoloration because of their dark hue and ability to adhere to dental surfaces.[19] The concern about bleaching in smokers also is highlighted by the eligibility criteria of several clinical trials on bleaching, which exclude smokers,[2-4,6,10,13,20-22] without scientific support that smoking can jeopardize the bleaching outcome.

Considering that the prevalence of self-assessed tooth discoloration in smokers is almost twice that reported by nonsmokers,[23] smokers are probably the main candidates for bleaching procedures. However, to our knowledge, no study investigators so far have evaluated whether smoking can affect bleaching effectiveness and TS. Therefore, our aim in this 2-center controlled clinical trial was to show the therapeutic equivalence of at-home bleaching in smokers and nonsmokers at 1 month (primary outcome) and 1 week (secondary outcome). In addition, we evaluated the absolute risk and intensity of TS.

METHODS

The State University of Ponta Grossa (protocol 16457/2012) and the University of Chile (protocol 2013/41) Ethics Committees approved this equivalence clinical trial. The ClinicalTrials.gov identification number was NCT02017873. The study took place within the dental clinics of both universities from February to December 2013.

Inclusion and exclusion criteria. We evaluated participants in a dental chair and after dental prophylaxis with pumice and water to check whether they met the study's eligibility criteria. Participants included in this clinical trial were aged between 18 and 54 years and had good general and oral health. Each participant had at least 1 central incisor of shade A2 or darker as assessed by means of comparison with a value-oriented shade guide (VITA classical, VITA Zahnfabrik). We did not include participants who had undergone previous dental bleaching procedures during orthodontic treatment or those who were pregnant or lactating or had bruxism habits. In addition, we excluded participants with restorations on the labial surfaces of their anterior teeth and noncarious cervical lesions; with veneers or full crowns; with gingival recession, spontaneous tooth pain, or internal tooth discoloration; and with teeth that had been treated endodontically or had fluorosis.

During screening, we measured the patients' baseline TS with vertical and horizontal percussion and with an air jet at the cervical area. We did not include patients with a TS higher than mild on a 5-point verbal numeric rating scale.

Sample size calculation. We based the sample size calculation on the color change measured with the spectrophotometer (ΔE), the primary outcome of the study. One hundred eighteen participants were required to exclude a difference of means of 2.0 units of ΔE at 1 week and 1 month (equivalence limit) with a power of 90% and α of 5%. With these calculations, we took into consideration a standard deviation of 3.3 in the ΔE. The equivalence limit we chose was lower than the ΔE threshold of 3.0, above which color differences become clinically perceptible.[24-26]

Study design. We asked the participants who met the inclusion criteria about their daily smoking habits. Those who did not smoke were part of the group of nonsmokers, and those who smoked at least 10 cigarettes per day belonged to the group of smokers. We included 60 participants in each group—30 from Brazil and 30 from Chile.

We made alginate impressions of each participant's maxillary and mandibular arch and filled the impressions with dental stone. We did not apply block-out material to the labial surfaces of the teeth.[27] We used a 1-millimeter–thick soft vinyl material provided by the manufacturer (Whiteness, FGM Dental Products) to fabricate the custom-fitted tray to hold the bleaching gel. We trimmed the bleaching tray 1 mm beyond the marginal gingiva and delivered the tray and the 10% CP gel (Whiteness Perfect, FGM Dental Products) to each participant with oral instructions for use. We instructed all participants to wear the tray with the bleaching agent for 3 hours daily for 3 weeks.

We instructed the participants to remove the tray after the daily bleaching period, wash it with water, and brush their teeth as usual. We also provided verbal instructions about oral hygiene, encouraging participants to brush their teeth regularly with fluoridated toothpastes without whitening components.

Shade evaluation. We evaluated the color with objective and subjective methods. For both devices, we checked the color at the middle one-third area of the labial surface of the anterior central incisor according to the American Dental Association guidelines.[28]

For the objective shade evaluation, we used a digital spectrophotometer (VITA Easyshade, VITA

ABBREVIATION KEY. **a*:** Color along the red-green axis. **b*:** Color along the yellow-blue axis. **CP:** Carbamide peroxide. **ΔE:** Color change measured with the spectrophotometer. **L*:** Luminosity. **NS:** Not significant. **ΔSGU:** Change in shade guide units. **TS:** Tooth sensitivity.

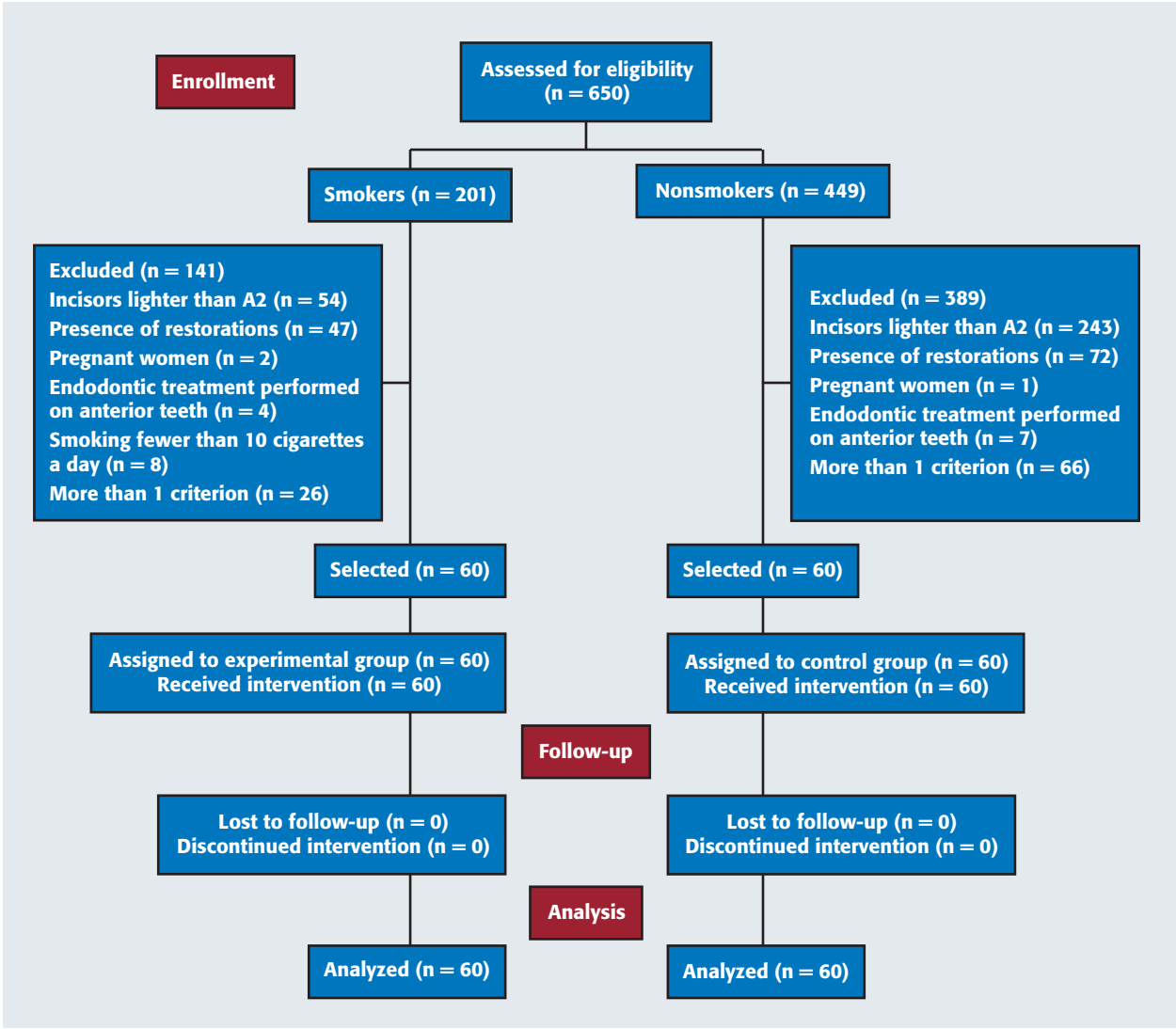

Figure. Flow diagram of the clinical trial, including detailed information regarding the excluded participants.

Zahnfabrik). For this purpose, we took an impression of the maxillary arch with dense silicone paste (Coltoflax and Perfil Cub, Vigodent), and we created a window on the labial surface of the silicone guide by using a metal device with a radius of 6 mm. The purpose of this procedure was to standardize the area for color evaluation in all recall periods with the spectrophotometer.

We determined the color using the parameters of the digital spectrophotometer on which the following values were indicated: L*, a*, and b*, where L* represents luminosity (the value from 0 [black] to 100 [white]), and a* and b* represent color along the red-green axis and color along the yellow-blue axis, respectively. We calculated the difference between baseline and each recall period (ΔE^*) by using the following formula[29]: $\Delta E^* = [(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2]^{1/2}$. For the subjective evaluation, we arranged the 16 tabs of the shade guide (VITA classical, VITA Zahnfabrik) from whitest to darkest as follows: B1, A1, B2, D2, A2, C1, C2, D4, A3, D3, B3, A3.5, B4, C3, A4, C4. Although this scale is not linear in the truest sense, we treated the changes as continuous, with a linear ranking as was used in several clinical trials on dental bleaching.[2,3,13,21] We calculated the color changes from the beginning of the active phase through the individual recall times by the change in shade guide units (ΔSGU) that occurred toward the lighter end of the value-oriented list of shade tabs. In the case of operator disagreement about color matching, we reached a consensus before dismissing the patient. Two calibrated evaluators in each center with a previous agreement of at

TABLE 1

Baseline characteristics of the participants.

CHARACTERISTIC	SMOKERS	NONSMOKERS
Age, y (Mean [SD]*)†		
Brazil	26.3 (6.5)	24.1 (6.8)
Chile	29.3 (9.4)	25.5 (6.6)
Male, %‡		
Brazil	63.3	53.3
Chile	63.3	36.7
Baseline Color, L* § (Mean [SD])¶		
Brazil	82.4 (4.9)	82.3 (4.3)
Chile	83.2 (4.0)	84.9 (3.8)
Baseline Color, b* # (Mean [SD])		
Brazil	22.6 (3.6)	23.2 (3.6)
Chile	22.2 (3.1)	21.7 (2.5)
Baseline Color, a* ** (Mean [SD])¶		
Brazil	−1.0 (1.0)	−0.5 (1.0)
Chile	−0.0 (0.7)	−0.2 (0.6)
Baseline Color, Shade Guide Units (Mean [SD])		
Brazil	6.8 (2.3)	7.4 (2.5)
Chile	7.2 (1.7)	8.4 (2.9)
Smoking Time, y (Mean [SD])		
Brazil	8 (5.9)	NS††
Chile	11.8 (9.1)	NS
Number of Cigarettes per Day (Mean [SD])		
Brazil	13.2 (4.0)	NS
Chile	12.8 (3.8)	NS

* SD: Standard deviation.
† Chileans and smokers were older (both $P = .002$).
‡ Smokers were more often male ($P = .040$).
§ L*: Luminosity.
¶ Chileans were 1.8 L* units lighter ($P = .018$) and −0.6 a* units lower ($P < .001$) than Brazilians.
# b*: Color along the yellow-blue axis.
** a*: Color along the red-green axis.
†† NS: Not significant.

least 85% determined by means of weighted κ statistics recorded the shade of the maxillary right central incisor at baseline, during treatment (after the first, second, and third weeks of bleaching), and 1 week and 1 month after the end of the bleaching protocol.

Participants' TS evaluation. We asked the participants to keep a daily record of whether they experienced TS by using a 5-point verbal numeric rating scale[4,30,31] and a visual analog scale.[3,12,32] For the numeric rating scale, we instructed the participants to choose 1 score from 0 to 4 to represent the intensity of the TS, with 0 indicating no TS; 1, mild TS; 2, moderate TS; 3, considerable TS; and 4, severe TS. For the visual analog scale, we instructed the participants to place a line perpendicular to a line 10 mm long with 0 at one end indicating no TS and at the 10-mm end indicating unbearable TS.

Statistical analysis. We performed all analyses by using software (SigmaPlot, Version 11.0, Systat Software and JMP, Version 11, SAS Institute) and a 5% significance level. We compared the baseline characteristics of SGU, L*, a*, b* and the patients' ages in both groups and centers by using a 2-way analysis of variance. We evaluated the percentage of male participants among the different groups and centers by using 2-way logistic regression.

We tested equivalent color change between the 2 groups at 1 month by using a multivariable model including the following study design variables: center (Chile versus Brazil), smoking (yes versus no), and the baseline shade evaluation. In addition, we tested the effect of age and sex. We calculated the 95% confidence interval (CI) for the difference from baseline for both the objective measure (ΔE) and the subjective measure (ΔSGU). We used the 2 1-sided tests procedure of Schuirmann[33] to show therapeutic equivalence if the difference between smokers and nonsmokers was within the preset boundaries of ± 2.0 units of ΔE at 1 month and at 1 week.

We also compared the baseline versus 1-week SGU of both groups by using a 2-way repeated measures analysis of variance. We performed this procedure to gather evidence about the effectiveness of whitening. We did not perform this procedure for ΔE because we did not have a baseline E value.

Similarly, we also used multivariable models, having the same study design variables described for color change, to compare the median TS values (numeric rating scale), mean visual analog scale, and risk of TS (presence or absence of TS at least once during treatment). We compared the absolute risk of TS of both groups by using χ^2 and Fisher exact tests, and the intensity of TS by using the Mann-Whitney test.

RESULTS

We screened 650 patients to obtain 120 participants who met the eligibility criteria. All participants included in this controlled clinical trial finished the bleaching protocol and attended all recall visits (Figure).

Baseline features. Table 1 presents the participants' baseline characteristics. We saw some slight differences in the baseline features between the 2 centers. Chileans were, on average, 2 years older ($P = .002$); 1.8 L* units lighter ($P = .018$), and −0.6 a* units lower (closer to the green; $P < .001$) than Brazilians. Smokers were, on average, 3 years older ($P = .002$), and more were male (63% versus 45%; $P = .040$). We anticipated these baseline differences in the study design and adjusted for them in the color change analysis.

Color change. Table 2 shows the color change measured 1 week and 1 month after bleaching for both

TABLE 2

Color change for both centers.

ASSESSMENT PERIOD	GROUP, MEAN (STANDARD ERROR)				DIFFERENCE	95% CONFIDENCE INTERVAL	EQUIVALENT*
	Smoker		Nonsmoker				
ΔE†							
Baseline Versus 1 Week	8.11	(0.349)	8.62	(0.349)	0.51	−0.48 to 1.49	Yes
Baseline Versus 1 Month	7.21	(0.401)	8.43	(0.401)	1.22	0.09-2.35	No
ΔSGU‡							
Baseline Versus 1 Week	4.21	(0.236)	4.22	(0.236)	0.01	−0.65 to 0.68	Yes
Baseline Versus 1 Month	4.04	(0.242)	4.13	(0.242)	0.08	−0.60 to 0.77	Yes

* Equivalent according to the 2 1-sided test after covarying out center and baseline color (luminosity, color along the yellow-blue axis, color along the red-green axis).
† ΔE: Color change measured with the spectrophotometer.
‡ ΔSGU: Change in shade guide units.

groups. In terms of ΔE, the overall color change at 1 month was mean 7.8 (standard deviation, 3.8) (95% CI, 7.1-8.5). We observed efficient whitening, with an overall color change at 1 month in SGU of 4.1 (2.4) (95% CI, 3.7-4.5) for all participants, regardless of the group. Significant difference in the baseline versus 1-week SGU ($P < .001$) for both groups is evidence of effective whitening (data not shown).

Because the 95% CI for the difference in color change between smokers and nonsmokers at 1 week was within the preset boundaries of ± 2.0 units of ΔE equivalence, at-home bleaching effectiveness was the same in smokers and nonsmokers for the 1-week data. However, this equivalence was not shown for the ΔE at 1 month because the 95% CI was not within the preset boundaries of ± 2.0 units.

TABLE 3

Parameter estimates from multivariable linear regression models at 1 month.

INDEPENDENT VARIABLE	ΔE*			ΔSGU†		
	Coefficient	Standard Error	*P* Value	Coefficient	Standard Error	*P* Value
Intercept	12.130	1.30	< .001	4.183	0.68	< .001
Smoking, Yes or No	0.496	0.62	.42	0.195	0.26	.46
Center	−3.789	0.60	< .001	−3.182	0.27	< .001
Baseline Color	NS‡	NS	NS	0.585	0.054	< .001

* R^2 for color change measured with the spectrophotometer = 0.317.
† R^2 for change in shade guide units = 0.657.
‡ NS: Not significant.

The multivariable regression analysis results indicated a significant relationship between color change and the study center (ΔE and ΔSGU) and the baseline color (ΔSGU) (Table 3). Age and sex were not predictors of the whitening outcome (data not shown). Changing the center was associated with a difference of 3.789 in the ΔE and 3.182 in the ΔSGU after adjusting for the other variables (Table 3). The model constructed for the ΔSGU also revealed a significant and positive effect of the baseline color. Every increase of 1 SGU in the baseline color resulted in an increase of approximately 0.6 in the final ΔSGU at 1 month.

Table 4 shows the effect of the center, with a significantly higher degree of whitening in the Brazil center ($P < .05$). The smoking condition (yes or no) did not affect the overall color change, without subgroup analysis, after 1 month in both models. Although we did not power the study to test for equivalence within all subgroups, equivalence was shown within all except ΔE in the Brazil center.

TS. In the nonsmoking group, 42% experienced TS at least once during the bleaching regimen, and in the smoking group 52% experienced TS (Table 5). This difference was not statistically significant (Fisher exact test, $P = .36$). The multivariable logistic regression analysis results revealed that none of the other independent variables were associated with TS after at-home bleaching (data not shown). Overall, the risk of TS was 47% (95% CI, 38-56%).

Similarly, TS intensity measured with the visual analog scale (Mann-Whitney test, $P = .26$) and the numeric rating scale (Mann-Whitney test, $P = .23$) was not significantly different between groups (Table 6). When TS was present, participants usually reported it as mild (score 1), and none of the patients from this trial abandoned the treatment.

DISCUSSION

A clear limitation of this 2-center controlled clinical trial is that neither the participants nor the evaluators were masked to the groups. In an attempt to mask the evaluators, we asked volunteers to rinse with a mouthwash before color evaluation. However, the smell of cigarettes

TABLE 4

Color change for each center.

ASSESSMENT PERIOD CENTER	GROUP, MEAN (STANDARD ERROR)		DIFFERENCE	95% CONFIDENCE INTERVAL	EQUIVALENT*
	Smoker	Nonsmoker			
ΔE†					
Baseline Versus 1 Week					
Brazil	9.66 (0.563)	10.43 (0.506)	0.76	−0.66 to 2.19	No
Chile	6.55 (0.525)	6.81 (0.532)	0.26	−1.12 to 1.65	Yes
Difference‡	3.12 (0.835)	3.62 (0.767)			
Baseline Versus 1 Month					
Brazil	7.82 (0.639)	10.05 (0.574)	2.23	0.61-3.85	No
Chile	6.58 (0.596)	6.84 (0.604)	0.26	−1.31 to 1.83	Yes
Difference‡	1.24 (0.948)	3.21 (0.871)			
ΔSGU§					
Baseline Versus 1 Week					
Brazil	5.13 (0.380)	5.48 (0.341)	0.36	−0.60 to 1.32	Yes
Chile	3.29 (0.354)	2.97 (0.359)	−0.31	−1.25 to 0.62	Yes
Difference‡	2.15 (0.567)	2.20 (0.509)			
Baseline Versus 1 Month					
Brazil	4.90 (0.389)	5.40 (0.349)	0.50	−0.48 to 1.49	Yes
Chile	3.17 (0.362)	2.86 (0.367)	0.31	−0.64 to 1.27	Yes
Difference‡	1.73 (0.576)	2.55 (0.529)			

* Equivalent according to the 2 1-sided test after covarying out center, center by smoking, and baseline color (luminosity, color along the yellow-blue axis, and color along the red-green axis). Smoking differences did not vary significantly according to center ($P > .05$).
† ΔE: Color change measured with the spectrophotometer.
‡ Brazilians had more color change ($P < .05$) than did Chileans.
§ ΔSGU: Change in shade guide units.

TABLE 5

Comparison of the number of patients who experienced tooth sensitivity at least once during the bleaching regimen in both groups.

SMOKING GROUP	NUMBER OF PARTICIPANTS WITH TOOTH SENSITIVITY		ABSOLUTE RISK (95% CONFIDENCE INTERVAL)*
	Yes	No	
Smokers	31	29	52 (39-63)
Nonsmokers	25	35	42 (30-54)

* χ^2 test ($P = .36$).

TABLE 6

Intensity of tooth sensitivity according to the 2 pain scales.

SMOKING GROUP	5-POINT VERBAL NUMERIC RATING SCALE*	VISUAL ANALOG SCALE†
Smokers	0 (0 or 1)	0.7 (1.2)
Nonsmokers	1 (0 or 1)	0.9 (1.4)

* Median (interquartile range); Mann-Whitney test ($P = .23$).
† Mean (standard deviation); Mann-Whitney test ($P = .26$).

was inevitable, and the examiners could guess which group each participant was from because of the impregnation of smoke smell in hair, hands, breath, and clothes.

The risk of TS with regard to at-home bleaching was not affected by smoking, study center, or any other independent variable collected in this trial. The overall risk of TS was reported to be 47%, which is within the range found in other studies in which the investigators used 10% CP as the bleaching agent.[4,6,8,9,11,12]

Although the risk of TS was high, affecting approximately one-half of the patients using at-home bleaching, TS intensity for both groups was mild, which is an advantage of at-home bleaching compared with the in-office procedure. TS intensity after in-office bleaching is usually moderate,[5,34-36] but, in some cases, is reported to be so severe that patients eventually abandon the procedure.[37]

Researchers are concerned about the possibility that alterations in tooth enamel caused by bleaching agents[14,16] may interfere negatively with treatment effectiveness. Results from laboratory studies have shown that bleaching agents promote alterations in the tooth enamel surface because of their slightly acidic nature[38] and demineralizing potential,[39] which could favor the greater retention of coloring agents in the enamel.

However, the results of our study contradict the widespread idea among clinicians that smoking can jeopardize the whitening produced by at-home bleaching. In our study, we observed that both study groups reached the same magnitude of color change 1 week after bleaching, being therefore equivalent in terms of whitening. The results of our study agree with those of an earlier study with results showing that coffee consumption during bleaching did not lessen the effectiveness of dental bleaching.[13]

Coffee, wine, and cigarette smoke are compounds composed of macromolecular chains and are, thus, not easily able to permeate human enamel, which allows the passage of only low-molecular-weight molecules.[40] These findings suggest that the dentin substrate on which CP exerts its oxidizing action is probably similar between

these study groups and does not seem to jeopardize the short-term bleaching outcome.

The lack of equivalence of ΔE at 1 month highlights that smokers are likely more susceptible to darkening due to the deposition of cigarette smoke components on the enamel surface. It is likely that this situation may worsen after some years, with smokers eventually having darker teeth than do nonsmokers. This finding cannot be interpreted as color rebound but is the result of the extrinsic staining on the enamel surface, which may be removed easily by means of mechanical cleaning.[41,42]

In our study, we observed an overall color change of approximately 4 SGU during the 3-week bleaching period. However, investigators in previous studies usually reported a greater color change of 5 to 6 SGU.[2,30,43] This difference in the magnitude of bleaching may be attributed to the significant effect of the study center on mean color change.

These results were surprising because we did not find articles published in the literature reporting the effects of ethnicity on bleaching outcome. Authors of a meta-analysis summarizing the database results collected as part of the development of a strip-based tooth-whitening system from 18 different clinical trials concluded that race and other factors such as baseline color are significant determinants of whitening effectiveness.[44] Investigators in another study reported significant differences regarding the degree of bleaching between whites and Hispanics.[45] The explanation for such differences due to ethnicity is yet to be investigated further.

CONCLUSIONS

The whitening outcome is not affected by smoking. Effective whitening is achieved regardless of whether the patient is a smoker. The magnitude of color change after at-home whitening is equivalent between smokers and nonsmokers at 1 week. Both groups achieved significant whitening with no differences in TS. However, this equivalence was not seen 1 month after bleaching, with smokers having slightly darker teeth than nonsmokers. Furthermore, long-term recalls should be performed to evaluate whether smoking affects the long-term effectiveness of bleaching. ■

Disclosure. None of the authors reported any disclosures.

This study was supported partially by grants 304105/2013-9 and 301891/2010-9 from the National Council for Scientific and Technological Development (Conselho Nacional de Desenvolvimento Científico e Tecnológico).

JADA's statistical editor Al M. Best III, PhD, provided assistance in the data analyses.

1. Kihn PW. Vital tooth whitening. *Dent Clin North Am*. 2007;51(2):319-331.

2. Meireles SS, Heckmann SS, Santos IS, Della Bona A, Demarco FF. A double blind randomized clinical trial of at-home tooth bleaching using two carbamide peroxide concentrations: 6-month follow-up. *J Dent*. 2008;36(11):878-884.

3. Bernardon JK, Sartori N, Ballarin A, Perdigão J, Lopes GC, Baratieri LN. Clinical performance of vital bleaching techniques. *Oper Dent*. 2010;35(1):3-10.

4. Türkün M, Celik EU, Aladağ A, Gökay N. One-year clinical evaluation of the efficacy of a new daytime at-home bleaching technique. *J Esthet Restor Dent*. 2010;22(2):139-146.

5. Basting LB, Amaral FLB, França FMG, Flório FM. Clinical comparative study of the effectiveness of and TS to 10% and 20% carbamide peroxide home-use and 35% and 38% hydrogen peroxide in-office bleaching materials containing desensitizing agents. *Oper Dent*. 2012;37(5):464-473.

6. de la Peña VA, Ratón ML. Randomized clinical trial on the efficacy and safety of four professional at-home tooth whitening gels. *Oper Dent*. 2013;39(1):136-143.

7. Haywood VB. Treating sensitivity during tooth whitening. *Compend Contin Educ Dent*. 2005;26(9 suppl 3):11-20.

8. Leonard RH Jr, Smith LR, Garland GE, et al. Evaluation of side effects and patients' perceptions during tooth bleaching. *J Esthet Restor Dent*. 2007;19(6):355-364.

9. Browning WD, Blalock JS, Frazier KB, Downey MC, Myers ML. Duration and timing of sensitivity related to bleaching. *J Esthet Restor Dent*. 2007;19(5):256-264.

10. Krause F, Jepsen S, Braun A. Subjective intensities of pain and contentment with treatment outcomes during tray bleaching of vital teeth employing different carbamide peroxide concentrations. *Quintessence Int*. 2008;39(3):203-209.

11. Meireles SS, Heckmann SS, Leida FL, Santos IS, Della Bona Á, Demarco FF. Efficacy and safety of 10% and 16% carbamide peroxide tooth-whitening gels: a randomized clinical trial. *Oper Dent*. 2008;33(6):606-612.

12. de Almeida LCAG, Costa CAS, Riehl H, dos Santos PH, Sundfeld R, Briso ALF. Occurrence of sensitivity during at-home and in-office tooth bleaching therapies with or without use of light sources. *Acta Odontol Latinoam*. 2012;25(1):3-8.

13. Rezende M, Loguercio AD, Reis A, Kossatz S. Clinical effects of exposure to coffee during at-home vital bleaching. *Oper Dent*. 2013;38(5):E229-E236.

14. Hosoya N, Honda K, Lino F, Arai T. Changes in enamel surface roughness and adhesion of *Streptococcus mutans* to enamel after vital bleaching. *J Dent*. 2003;31(8):543-548.

15. Espina VT, Larentis NL, Souza MAL, Barbosa NA. Comparação da superfície do esmalte antes e após o clareamento com dois diferentes agentes: estudo clínico. *Stomatos*. 2008;14(27):44-52.

16. Bodanezi A, de Bittencourt ME, Bodanezi RV, Zottis T, Munhoz EA, Carlini B Jr. Surface modifications on aesthetically restored teeth following home bleaching with 16% peroxide carbamide. *Eur J Dent*. 2011;5(2):157-162.

17. Cândido AP, Araújo JTL, Silva CHV, Souza FB, Guimarães RP. Avaliação da permeabilidade do esmalte exposto a diferentes concentrações de peróxido de hidrogênio e peróxido de carbamida. *Odontol Clín-Científ*. 2005;4(3):207-211.

18. Wasilewski Mde S, Takahashi MK, Kirsten GA, de Souza EM. Effect of cigarette smoke and whiskey on the color stability of dental composites. *Am J Dent*. 2010;23(1):4-8.

19. Bertoldo CES, Miranda DA, Souza-Júnior EJ, et al. Surface hardness and color change of dental enamel exposed to cigarette smoke. *Int J Dent Clin*. 2011;3(4):1-4.

20. Grobler SR, Hayward R, Wiese S, Moola MH, van W Kotze TJ. Spectrophotometric assessment of the effectiveness of Opalescence PF 10%: a 14-month clinical study. *J Dent*. 2010;38(2):113-117.

21. Jadad E, Montoya J, Arana G, Gordillo LAA, Palo RM, Loguercio AD. Spectrophotometric evaluation of color alterations with a new dental bleaching product in patient wearing orthodontic appliances. *Am J Orthod Dentofacial Orthop*. 2011;140(1):e43-e47.

22. Bonafé E, Bacovis CL, Iensen S, Loguercio AD, Reis A, Kossatz S. Tooth sensitivity and efficacy of in-office bleaching in restored teeth. *J Dent*. 2013;41(4):363-369.

23. Alkhatib MN, Holt RD, Bedi R. Smoking and tooth discolouration: findings from a national cross-sectional study. *BMC Public Health*. 2005;5:27.

24. Ruyter IE, Nilner K, Moller B. Color stability of dental composite resin materials for crown and bridge veneers. *Dent Mater*. 1987;3(5):246-251.

25. Johnston JG, Kao EC. Assessment of appearance match by visual observation and clinical colorimetry. *J Dent Res*. 1989;68(5):819-822.

26. Um CM, Ruyter IE. Staining of resin-based veneering materials with coffee and tea. *Quintessence Int*. 1991;22(5):377-386.

27. Matis BA, Hamdan YS, Cochran MA, Eckert GJ. A clinical evaluation of a bleaching agent used with and without reservoirs. *Oper Dent*. 2002; 27(1):5-11.

28. American Dental Association. Acceptance Program Guidelines. Dentist dispensed home-use tooth bleaching products. April 2006. Available at: http://www.ada.org/~/media/ADA/Science%20and%20Research/Files/guide_home_bleach.ashx. Accessed December 18, 2014.

29. Commission Internationale de l'Eclairage. *Recommendations on Uniform Color Spaces, Color Difference Equations, Psychometric Color Terms*. Supplement 2 to CIE Publication 15 (E2-31.1)1971 (TC-1.3)1978. Paris, France: Bureau Central de la CIE; 1978.

30. Cardoso PC, Reis A, Loguercio A, Vieira LC, Baratieri LN. Clinical effectiveness and tooth sensitivity associated with different bleaching times for a 10 percent carbamide peroxide gel. *JADA*. 2010;141(10):1213-1220.

31. Kose C, Reis A, Baratieri LN, Loguercio AD. Clinical effects of at-home bleaching along with desensitizing agent application. *Am J Dent*. 2011;24(6):379-382.

32. Da Costa JB, McPharlin R, Hilton T, Ferracane JL, Wang M. Comparison of two at-home whitening products of similar peroxide concentration and different delivery methods. *Oper Dent*. 2012;37(4):333-339.

33. Schuirmann DJ. A comparison of the two one-sided tests procedure and the power approach for assessing the equivalence of average bioavailability. *J Pharmacokinet Biopharm*. 1987;15(6):657-680.

34. Kossatz S, Martins G, Loguercio AD, Reis A. Tooth sensitivity and bleaching effectiveness associated with use of a calcium-containing in-office bleaching gel. *JADA*. 2012;143(12):e81-e87.

35. Ozcan M, Abdin S, Sipahi C. Bleaching induced tooth sensitivity: do the existing enamel craze lines increase sensitivity? A clinical study. *J Odontol*. 2013;102(2):197-202.

36. Paula E, Kossatz S, Fernandes D, Loguercio A, Reis A. The effect of perioperative Ibuprofen use on tooth sensitivity caused by in-office bleaching. *Oper Dent*. 2013;38(6):601-608.

37. do Amaral FL, Sasaki RT, da Silva TC, França FM, Flório FM, Basting RT. The effects of home-use and in-office bleaching treatments on calcium and phosphorus concentrations in tooth enamel: an in vivo study. *JADA*. 2012;143(6):580-586.

38. Freire A, Archegas LR, de Souza EM, Vieira S. Effect of storage temperature on pH of in-office and at-home dental bleaching agents. *Acta Odontol Latinoam*. 2009;22(1):27-31.

39. Tanaka R, Shibata Y, Manabe A, Miyazaki T. Micro-structural integrity of dental enamel subjected to two tooth whitening regimes. *Arch Oral Biol*. 2010;55(4):300-308.

40. Nicholson JW. Biologic considerations. In: Schwartz RS, Summitt JB, Robbins JW, Santos J, eds. *Fundamentals of Operative Dentistry: A Contemporary Approach*. Hanover Park, IL: Quintessence Publishing; 1996:1-25.

41. Kalyana P, Shashidhar A, Meghashyam B, Sreevidya KR, Sweta S. Stain removal efficacy of a novel dentifrice containing papain and Bromelain extracts: an in vitro study. *Int J Dent Hyg*. 2011; 9(3):229-233.

42. Bazzi JZ, Bindo MJF, Rached RN, Mazur RF, Vieira S, de Souza EM. The effect of at-home bleaching and toothbrushing on removal of coffee and cigarette smoke stains and color stability of enamel. *JADA*. 2012;143(5): e1-e7.

43. Bizhang M, Chun YHP, Damerau K, Singh P, Raab WHM, Zimmer S. Comparative clinical study of the effectiveness of three different bleaching methods. *Oper Dent*. 2009;34(6):635-641.

44. Zhou X, Barker ML, Gibb RD, Gerlach RW. Impact of behavioral, clinical and demographic parameters on whitening response: evidence from 18 clinical trials. Research presented at: 80th General Session and Exhibition of the International Association for Dental Research. March 6-9, 2002; San Diego, CA.

45. Li Y, Komora DA, Kubrock KM, Royer JS, Lee SS, Kim JS. Tooth bleaching efficacy and age, gender, ethnicity and smoking. Research presented at: 84th General Session and Exhibition of the International Association for Dental Research. June 28 - July 1, 2006; Brisbane, Australia.