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ORIGINAL ARTICLE

Bleaching efficacy and quality of life of different bleaching techniques — randomized controlled trial

Ruben Pereira[1] · João Silveira[2] · Susana Dias[1] · Ana Cardoso[1] · António Mata[2] · Duarte Marques[2]

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Abstract

Objectives To evaluate bleaching efficacy and oral health-related quality of life (ORHQoL) of three bleaching systems with similar hydrogen peroxide (HP) concentration for up to 6 months post-treatment.

Materials and methods A randomized controlled trial was designed with three parallel groups: group A — in-office 6% HP paint-on varnish; group B — at-home 6% HP with adaptable tray; group C — at-home 16% carbamide peroxide with custom tray. At three different stages (baseline, after bleaching, and 6-month follow-up), ORHQoL was evaluated by the OHIP-14 questionnaire and tooth color of the upper canines and central incisors were measured by two shade guides and a spectrophotometer (measuring CIE L*a*b* with respective color/whiteness differences – $\Delta E_{00}/\Delta WI_D$). Results were presented as mean and 95% confidence intervals and statistical tests were performed appropriately, considering a significance level of $\alpha = 0.05$.

Results All groups presented significant color differences ($P < 0.05$) between all stages, with $\Delta E_{00}/\Delta WI_D$ surpassing the perceptibility threshold in 98% cases, with group C's results being significantly ($P < 0.05$) higher when compared to other groups, although with significantly ($P < 0.05$) higher values of color relapse. Significative ORHQoL improvements ($P < 0.05$) were detected after bleaching in a global analysis with no differences between techniques.

Conclusions All techniques presented bleaching efficacy, color stability, and improvements in ORHQoL up to 6 months post-treatment.

Clinical significance Clinicians may consider both at-home and in-office bleaching techniques with 6% HP to attain long-lasting satisfactory clinical results while producing positive changes in ORHQoL.

Keywords Tooth bleaching · Tooth bleaching agents · Color · Aesthetics · Quality of life

Introduction

Patients seek care from dental professionals for preventive treatments or to address their current oral health problems. Common concerns regard the appearance and color of their teeth, as dissatisfaction with tooth color is widely reported in several adult populations, ranging from 19.6 to 65.9% [1–3]. This dissatisfaction has led to an increased desire for treatments that improve dental aesthetics, including tooth bleaching, which is a conservative and viable option for attaining a patient's desired smile when tooth integrity is acceptable [1, 4, 5].

Tooth bleaching can be performed at home or in the dental office by a wide range of techniques [4, 6]. At-home bleaching has become increasingly popular since the introduction of the nightguard vital bleaching in 1989, which is the most prescribed technique among dentists, mainly due to its high efficacy and safety profile [5, 7–13]. Although the described protocol for at-home bleaching is the overnight use of a custom tray with a 10% carbamide peroxide (CP) gel (which requires medical prescription), nowadays, several modifications and formulations can be found among manufacturers, with application times ranging between 1 and 8 hours a day [14, 15].

As an alternative to at-home bleaching, dentists can perform in-office techniques which are viable options typically associated

✉ Duarte Marques
duarte.marques@campus.ul.pt

[1] Oral Biology and Biochemistry Research Group, Faculdade de Medicina Dentária, Universidade de Lisboa, Lisbon, Portugal

[2] Oral Biology and Biochemistry Research Group - LIB-Phys FCT UID/FIS/04559/2013, Faculdade de Medicina Dentária, Universidade de Lisboa, Lisbon, Portugal

with higher hydrogen peroxide (HP) concentrations. Most of the products have 35% to 40% HP and are available in the form of a base and catalyst gel, either ready-mixed or supplied as a powder/liquid combination to be freshly mixed at the dental office [16–19]. The rationale for those higher HP concentrations lies in obtaining faster results, thus being indicated for situations when immediate whitening is required [16, 20]. However, HP's oxidative properties prompted manufacturers and clinicians to search for in-office techniques with lower HP concentrations to prevent hazardous effects on biological tissues [6, 21–23]. As a result, a wide range of bleaching products with lower peroxide concentrations have been developed over the years, and even an at-home paint-on varnish technique (VivaStyle Paint On Plus, Ivoclar Vivadent, Liechtenstein) was proposed for in-office use due to its fast-bleaching rate suggested by a fast HP release in approximately 10 min [18, 24–26]. Although evidence shows promising efficacy results (tooth color change), many issues have not yet been addressed as no studies have compared this proposed technique with at-home techniques [27, 28]. Concomitantly, studies lack evidence regarding tooth color stability, which is a great concern since tooth color relapses are common issues that may require touch-up bleaching [4, 29–33].

The quantitative analysis of tooth color changes and stability is important to evaluate the efficacy/effectiveness of a bleaching technique; however, patient-reported outcomes are also major aspects of a successful treatment and can be characterized by changes in oral health-related quality of life (OHRQoL) [34–37]. Currently, tooth bleaching is known to potentially influence OHRQoL by affecting the patient's self-esteem and social behaviors, such as smiling, laughing, or showing teeth without embarrassment [34, 35]. Therefore, the long-term effects of tooth bleaching are not only related to tooth color stability but may also impact the patient's everyday life.

This study aimed to compare the bleaching efficacy and OHRQoL of three different bleaching systems with a similar HP concentration of 6% or its CP equivalent while assessing the outcomes for up to 6 months. The following null hypotheses were established: (1) there were no differences in bleaching efficacy between the three tested bleaching systems; (2) there were no differences in tooth color stability, at the 6-month follow-up, between the three tested bleaching systems; (3) there were no differences in OHRQoL, at the end of treatment, between the three tested bleaching systems; (4) there were no differences in OHRQoL, at the 6-month follow-up, between the three tested bleaching systems.

Materials and methods

This randomized clinical trial took place between November 2019 and October 2021 at the Faculty of Dental Medicine of the University of Lisbon and was conducted in full compliance with the Helsinki World Medical Association Declaration's most recent amendments [38]. Additionally, the local ethics committee gave ethical approval, and the trial was registered at the U.S. National Library of Medicine ClinicalTrials.gov website under the reference number NCT03588871.

Study design and participants

A randomized clinical trial was designed with three parallel groups corresponding to different products and techniques: group A, in-office paint-on varnish 6% HP (VivaStyle Paint On Plus, Ivoclar Vivadent, Liechtenstein); group B, at-home 6% HP with a prefilled disposable tray (Opalescence GO, Ultradent, EUA); group C, at-home 16% CP with a customized tray (Opalescence PF 16% CP, Ultradent, EUA).

Participants attending the faculty clinic were screened according to the following inclusion criteria and consecutively recruited: being at least 18 years of age, having the upper canines darker than A3.5 in VITA Classical (VC) shade guide (assessed by spectrophotometry), accepting to interrupt smoking habits during the full duration of the study, and signing an informed consent form. The exclusion criteria were the presence of fixed orthodontic appliances, decayed teeth, pregnancy, poor oral hygiene, anterior teeth (16 anterior teeth, from the second premolar to the second premolar) with dental restorations, endodontic treatment, and severe anomalies of the dental structure or intrinsic stain. A flowchart of the study is summarized in Fig. 1.

Randomization process and blinding

Each bleaching system was coded from A to C using a randomization software (GraphPad QuickCals, http://www.graphpad.com/quickcalcs/randomize1.cfm), and the information was held by external personnel until the end of the study. A third party (blinded to the allocation results) analyzed the data in an SPSS worksheet (IBM Statistics, Inc., Chicago, IL, USA) where each bleaching system was referred to as groups A to C.

Participant and clinical operator blinding was not possible due to the three whitening systems' different formulations. However, the tooth color examiners were blinded, and spectrophotometric analysis is not susceptible to interpretation, thus reducing the potential bias.

Calibration of examiners for clinical analysis

Visual shade selection was performed by dentists with at least 5-year clinical experience and negative history of visual color deficiencies (confirmed using X-Rite Color Challenge by Pantone®) who were submitted to a calibration process. This

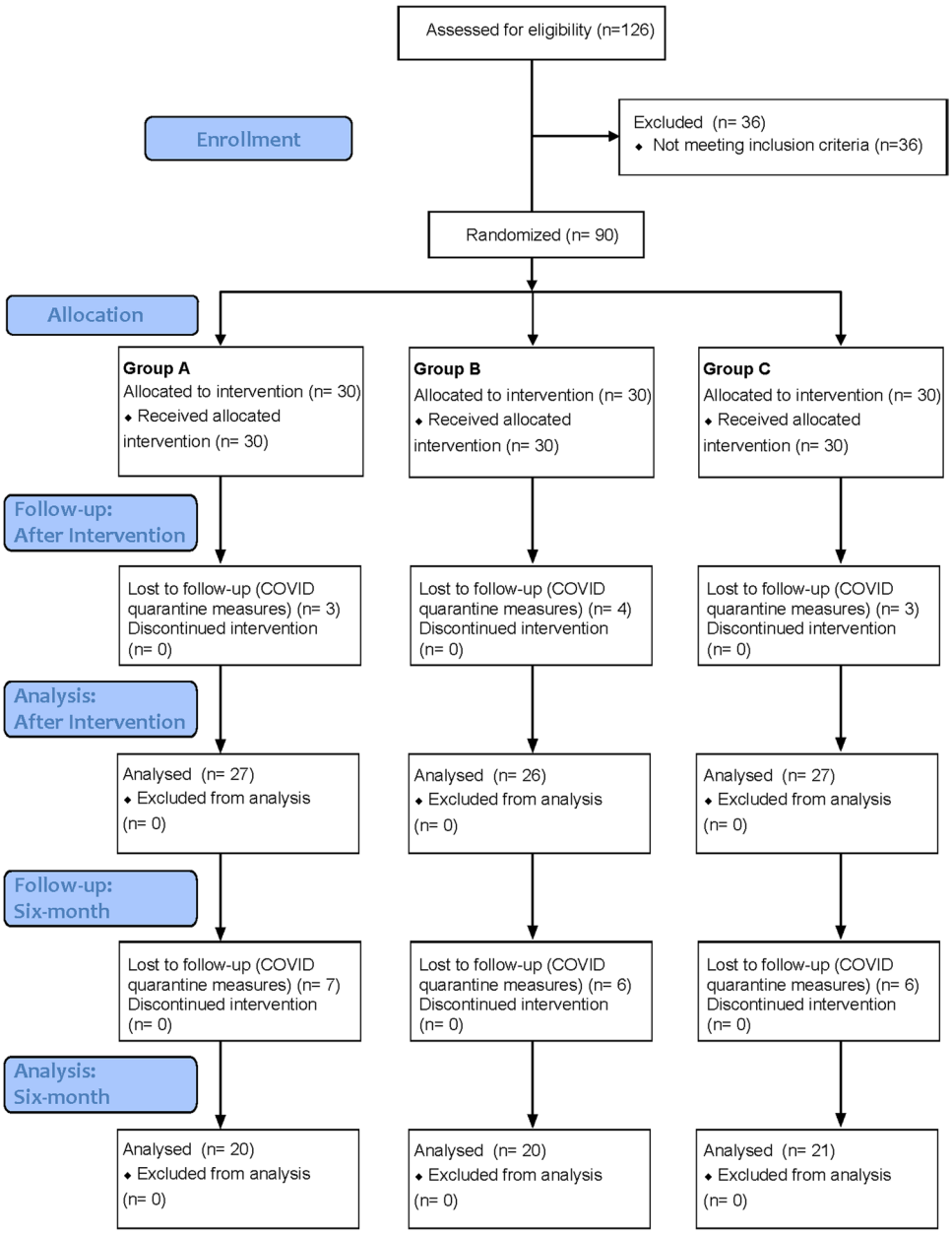

Fig. 1 Flowchart of the study, according to CONSORT

process was based on a consecutive determination of VITA Classical (VC) visual shade guides using two VC scales (one of which had a blinded identification; VITA Zahnfabrick, Germany). The dentist would be considered a valid operator with an intraclass correlation coefficient (ICC; model: two-way random; type: absolute agreement) higher than 0.80 (considered excellent agreement [39]). The same process was repeated for the VITA Bleachedguide 3D-Master shade guide (VB) (VITA Zahnfabrick, Germany). The calibrated operators' ICC ranged between 0.86 and 0.93. During the study, if disagreements occurred, the examiners reached a consensus. To standardize lighting conditions, the Smile Lite device (Smile Line AS, Switzerland; serial number 052015) with LED lights at 5500 K and a polarization filter was used.

An independent and blinded examiner performed objective tooth color measurements with a spectrophotometer, SpectroShade micro (SS) (MHT Optic Research, Niederhasli, Switzerland; serial number HDL3973), which is considered a diagnostic device for tooth color assessment [40–43]. The SS intradevice's calibration process was performed before each measuring round according to the manufacturer's instructions.

Oral health-related quality of life evaluation

The validated Portuguese version of the Oral Health Impact Profile 14 (OHIP-14) was applied at baseline, at the end of treatment (after bleaching), and after 6 months (6-month

follow-up) [44]. The questionnaire consisted of 14 questions with seven domains (2 questions per domain): functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap. The answers were scored according to a Likert scale [45] from 0 to 4 (never = 0, rarely = 1, sometimes = 2, repeatedly = 3, always = 4), with higher scores representing a worse OHRQoL (OHIP-14 total score ranged from 0 to 56 and each domain score from 0 to 8). Effect size (ES; calculated by Kendall's *W*) and standardized response mean (SRM; calculated by dividing the mean score change by the standard deviation of the change) were calculated as previously recommended for health questionnaires (ES and SRM were described as small < 0.3, moderate 0.3–0.8, or large ≥ 0.8 effect) [46–48]. A minimal important difference (MID) of five in the total OHIP-14 score change was also considered [46, 49].

The OHIP-14 was applied twice to each participant with a 1-week interval before bleaching treatment to evaluate the questionnaire's reliability and internal consistency. Test–retest reliability was evaluated for each question by ICC (model: two-way random; type: absolute agreement) with values ranging from 0.51 (moderate agreement) to 0.74 (substantial agreement) [39]. Internal consistency was evaluated by Cronbach's alpha with an obtained value of 0.81, which is desirable and considered good consistency [50].

Clinical procedures and measurements

In the first appointment, each patient was screened according to the previously described inclusion/exclusion criteria and submitted to professional dental prophylaxis with interproximal radiographs for diagnosis purposes. The professional dental prophylaxis was performed using an ultrasonic scaler and a nylon brush with prophylaxis paste (Cleanic, Kerr Orange, USA) in a low-rotation contra-angle handpiece by a dentist. Each patient was assigned to one group, according to the randomization process. One week after, the clinical bleaching protocol was performed according to the technique's description (Table 1) [4, 24, 27, 51].

To assess tooth sensitivity that could lead to treatment interruption, all patients were instructed to fill a daily visual analogic scale (VAS) form during the treatment (15 days), numbered from 0 (no pain) to 10 (maximum extreme pain), while notifying medication intake and oral lesions occurrences. Additionally, instruction forms were delivered with information regarding at-home bleaching procedures, food intake (to avoid acidic and potential staining foods), and oral hygiene. Patients were instructed to use their regular toothpaste during the whole study to avoid any potential change in tooth sensitivity unless it was a whitening toothpaste, in which case they were instructed to change to a non-whitening 1450-ppm fluoride-containing toothpaste.

Tooth color measurements were performed at baseline, after bleaching treatment, and at the 6-month follow-up. The color of the upper central incisors and canines' buccal surfaces was assessed with the VC and VB shade guides with the patient seated in the high Fowler's position on the dental chair while the calibrated examiner used the Smile Lite device with LED lights at 5500 K and a polarization filter for standard lighting conditions. The shade tabs received a number to categorize each color: VC tabs were numbered from 1 to 16 according to the color's value order from the highest (B1) to lowest (C4), and VB tabs were also numbered according to the color's value order from 1 to 15 (highest: 0M1; lowest: 5M3). An interpolated guide corresponding to the American Dental Association's Eq. (1 ccu = 1; SGU = 1 ΔE; ccu, color difference unit; SGU, shade guide unit; ΔE, overall color difference) was used to express results in shade guide units, and the differences were expressed by ΔSGU (SGU_{VC} and ΔSGU_{VC} for the VC shade guide; SGU_{VB} and ΔSGU_{VB} for the VB shade guide) [36, 52]. The SS performed three measuring replicates to obtain the CIE L*a*b* values of the upper central incisors and canines' buccal surfaces, following the manufacturer's instructions. The total tooth color difference (ΔE_{00}) and tooth whiteness index (WI_D), with the corresponding difference (ΔWI_D), both based on the CIE L*a*b* color notation system, were calculated to evaluate bleaching efficacy at the end of treatment and color relapse at the 6-month follow-up [53–56].

Sample size calculation

The sample size was calculated based on the upper canines' color difference (ΔE_{00} — a primary outcome) recorded in a previously performed pilot study with 30 randomized

Table 1 Simplified clinical protocol for each bleaching product. *HP*, hydrogen peroxide; *CP*, carbamide peroxide

Bleaching product	Clinical protocol
Group A VivaStyle Paint On Plus 6% HP	In-office applications: 2 sessions with 6 applications of 10 min with a 1-week interval (2 h application time)
Group B Opalescence GO 6% HP	At-home applications: 1 daily application of 90 min for 10 days (15 h application time)
Group C Opalescence PF 16% CP	At-home applications: 1 daily application of 6 h for 14 days (84 h application time)

participants (GraphPad QuickCals, http://www.graphpad.com/quickcalcs/randomize1.cfm), using the G*Power 3.1 software (Heinrich-Heine-Universität, Düsseldorf, Germany). The size effect was calculated based on the perceptibility threshold $\Delta E_{00} = 0.8$ with a standard deviation of 0.81 [57, 58]. Considering an *F* test (one-way ANOVA) with a significance level of 5% and a power of 80%, a minimum of 20 participants per group was required. To offset a possible attrition bias, 50% was added to each group, resulting in 30 patients' samples (a total of 90 patients).

Statistical analysis

All collected data were analyzed using IBM SPSS version 25 (IBM Statistics, Inc. Chicago, IL, USA). Results are presented as mean and 95% confidence interval (IC) of CIE L*a*b* color parameters, SGU, and OHIP-14 scores, with the respective WI_D, ΔE_{00}, ΔWI_D, and ΔSGU calculated. The CIEDE2000 formula from the Commission Internationale De l'Eclairage (CIE, International Commission on Illumination) was used to calculate ΔE_{00}. Computations with this color difference formula were performed according to the following equation [56]:

$$\triangle E_{00} = \sqrt{\left(\frac{L_2 - L_1}{K_L S_L}\right)^2 + \left(\frac{C_2 - C_1}{K_C S_C}\right)^2 + \left(\frac{H_2 - H_1}{K_H S_H}\right)^2 + R_T\left(\frac{C_2 - C_1}{K_C S_C}\right)\left(\frac{H_2 - H_1}{K_H S_H}\right)}$$

The variables of the CIEDE2000 formula were calculated from the CIE L*a*b* values using a free online code while setting the parametric factors to 1 (https://www.rit.edu/cos/colorscience/rc_useful_data.php).

The whiteness index was calculated before and after tooth bleaching with the following formula: $WI_D = 0.511L^* - 2.324a^* - 1.100b^*$ [54]. Color and whiteness difference perception was assessed according to two major thresholds: perceptibility threshold (PT for ΔE_{00}; WPT for ΔWI_D) considered $\Delta E_{00} = 0.8$ and $\Delta WI_D = 0.72$; acceptability threshold (AT for ΔE_{00}; WAT for ΔWI_D) considered $\Delta E_{00} = 1.8$ and $\Delta WI_D = 2.60$ [55, 58]. The percentages of cases in which ΔE_{00} and ΔWI_D were higher than the respective thresholds were calculated, and the bleaching efficacy was considered when both perceptibility thresholds were surpassed. When comparing post-treatment results with the 6-month follow-up, surpassing of both perceptibility thresholds was considered a tooth color relapse. The surpassing of both acceptability thresholds at the 6-month follow-up compared to the baseline values was considered undoubted color differences with no requirement for touch-up bleaching.

Since darker-colored teeth may have a different response to tooth bleaching, the upper central incisors and canines were analyzed in individual groups. Statistical analysis was performed with parametric tests whenever the minimal sample of 30 was attained according to the central limit theorem [59]. The variables without a minimal sample of 30 were evaluated regarding their distribution with the Kolmogorov–Smirnov test, and non-parametric tests were used to analyze the OHIP-14 score (results were also presented with median values). Repeated-measures analysis of variance (ANOVA) with Tukey post hoc test was performed to analyze intragroup differences at different times (baseline, after bleaching, and 6-month follow-up) in CIE L*a*b*, WI_D, and SGU, while the one-way ANOVA with Tukey post hoc test analyzed intergroup differences in ΔE_{00}, ΔWI_D, and ΔSGU. Differences in the OHIP-14 score among different times were determined by the Friedman test, while the Kruskal–Wallis test was adopted for multiple group comparison. In all statistical tests, the level of significance considered was 5%.

Results

Ninety participants were included in the study after the recruitment procedures: 56 females and 24 males, aged between 18 and 40 years old with a mean of 23.0 [22.8:23.4] years. A total of 80 bleaching treatments were completed (group A: 27; group B: 26; group C: 27) with an overall 11.1% attrition bias due to COVID-19 quarantine measures, leading to an overall 32.2% attrition bias at the 6-month follow-up (group A: 20; group B: 20; group C: 21) (Fig. 1). Baseline CIE L*a*b*, WI_D, and SGU values are depicted in Table 2 and did not show significant ($P > 0.05$) differences between groups, resulting in tooth-color and whiteness homogeneity before bleaching treatment.

Bleaching efficacy analysis (depicted in Table 3) detected that the perceptibility thresholds (PT and WPT) in all techniques were surpassed in at least 98% of cases and attained 100% in the upper canines (98% for acceptability thresholds). Thus, all techniques showed bleaching efficacy even though the $\Delta E_{00}/\Delta WI_D/\Delta SGU$ were significantly higher ($P < 0.05$) in group C after bleaching. Concomitantly, the ANOVA also detected significant differences ($P < 0.05$) in all groups' CIE L*a*b*, WI_D, and SGU (both VC and VB) values after bleaching (depicted in Table 2). The L* color coordinate presented significantly ($P < 0.05$) higher mean values while a* and b* were lower when compared to baseline, indicating a lighter and less yellow tooth color post-treatment. The WI_D mean values were significantly ($P < 0.05$) higher after bleaching in all groups, thus indicating increased levels of whiteness in tooth color. The SGU_{VC} and SGU_{VB} mean values were significantly ($P < 0.05$) lower after bleaching, indicating that the examiners detected higher value color tabs.

At the 6-month follow-up, an inverse response was detected in all variables, with values becoming closer to

Table 2 Mean and 95% IC values for CIE L*a*b*, WI_D, SGU_{VC}, and SGU_{VB} at different times. In all groups, the repeated measures ANOVA with Tukey post hoc presented statistically significant ($P < 0.05$) intragroup differences between baseline, after bleaching, and 6-month follow-up evaluations

		Baseline 80 cases			After bleaching 80 cases			6-month follow-up 61 cases		
		Group A 27 cases $n=54$	Group B 26 cases $n=52$	Group C 27 cases $n=54$	Group A 27 cases $n=54$	Group B 26 cases $n=52$	Group C 27 cases $n=54$	Group A 20 cases $n=40$	Group B 20 cases $n=40$	Group C 21 cases $n=42$
L*	Canines	70.6 [70.1:71.1]	70.0 [69.6:70.3]	70.0 [69.1:70.2]	74.3 [73.8:74.7]	74.1 [73.6:74.6]	76.3 [75.6:77.0]	73.6 [73.1:74.2]	73.9 [73.4:74.4]	75.6 [75.0:76.2]
	Incisors	75.7 [75.3:76.1]	75.7 [75.3:76.2]	75.3 [74.7:75.8]	77.8 [77.4:78.2]	77.4 [77.0:77.9]	78.4 [77.8:78.9]	77.0 [76.4:77.6]	77.4 [77.0:77.8]	78.1 [77.5:78.7]
a*	Canines	5.1 [4.9:5.3]	5.4 [5.2:5.5]	5.3 [5.1:5.6]	3.6 [3.4:3.8]	3.3 [3.1:3.6]	2.4 [2.1:2.6]	3.5 [3.3:3.7]	3.5 [3.2:3.7]	2.5 [2.3:2.7]
	Incisors	2.1 [2.0:2.3]	2.2 [2.0:2.3]	2.3 [2.0:2.5]	1.6 [1.5:1.7]	1.5 [1.3:1.6]	1.3 [1.2:1.5]	1.6 [1.4:1.7]	1.5 [1.4:1.6]	1.2 [1.0:1.3]
b*	Canines	24.1 [23.5:24.6]	24.0 [23.5:24.5]	23.9 [23.2:24.6]	19.3 [18.7:19.8]	19.7 [18.9:20.4]	15.0 [14.3:15.8]	20.2 [19.6:20.8]	20.2 [19.5:20.9]	16.4 [15.8:16.9]
	Incisors	17.6 [17.1:18.2]	17.0 [16.4:17.7]	17.2 [16.6:17.9]	14.7 [14.1:15.1]	14.2 [13.5:14.8]	12.0 [11.4:12.6]	20.2 [19.6:20.8]	20.2 [19.5:20.9]	16.4 [15.8:16.9]
WI_D	Canines	−2.3 [−3.4:−1.2]	−3.1 [−3.9:−2.2]	−2.5 [−4.3:−0.6]	8.4 [7.4:9.5]	9.0 [7.8:10.2]	17.8 [16.7:18.9]	7.2 [6.1:8.3]	7.4 [6.1:8.8]	14.7 [13.6:15.8]
	Incisors	14.3 [13.3:15.3]	14.9 [13.7:16.1]	14.2 [12.8:15.6]	19.9 [19.2:20.6]	20.8 [19.0:21.8]	24.3 [23.4:25.1]	17.5 [15.9:19.1]	19.7 [18.7:20.8]	22.7 [21.8:23.5]
SGU_{VC}	Canines	12.1 [11.9:12.4]	11.9 [11.5:12.3]	12.0 [11.7:12.2]	4.5 [4.1:5.1]	5.1 [4.8:5.6]	2.9 [2.6:3.3]	7.2 [6.1:8.3]	7.4 [6.1:8.8]	14.7 [13.6:15.8]
	Incisors	4.9 [4.4:5.4]	4.2 [3.6:4.8]	4.1 [3.7:4.5]	1.3 [1.1:1.4]	1.6 [1.4:1.9]	1.0 [1.0:1.8]	17.5 [15.9:19.1]	19.7 [18.7:20.8]	22.7 [21.8:23.5]
SGU_{VB}	Canines	10.9 [10.7:11.1]	10.9 [10.6:11.1]	10.7 [10.5:10.9]	6.8 [6.5:7.1]	6.7 [6.3:7.1]	4.8 [4.5:5.1]	7.2 [6.1:8.3]	7.4 [6.1:8.8]	14.7 [13.6:15.8]
	Incisors	6.8 [6.5:7.1]	6.2 [5.7:6.7]	6.5 [6.2:6.8]	3.7 [3.5:3.9]	3.6 [3.3:3.9]	2.8 [2.5:3.0]	17.5 [15.9:19.1]	19.7 [18.7:20.8]	22.7 [21.8:23.5]

the respective baseline. However, significant differences ($P < 0.05$) were still detected in $\Delta E_{00}/\Delta WI_D/\Delta SGU$ (Table 3) and CIE L*a*b*, WI_D, and SGU (Table 2), with a maximum of 16.7% of cases needing touch-up bleaching (evaluated by the acceptability thresholds). Thus, all techniques showed color stability even though tooth color relapse cases were higher in group C (83.3% cases) with significantly superior ($P < 0.05$) $\Delta E_{00}/\Delta WI_D$ values compared to after bleaching.

There were no reports of treatment interruption due to tooth hypersensitivity or presence of oral lesions, with the following overall VAS mean values: 1.0 [0.6:1.5] in group A, 1.2 [0.7:1.7] in group B, and 1.6 [0.9:2.2] in group C, without significant ($P > 0.05$) differences in the ANOVA. Oral lesions were reported in eight out of 27 cases in group A, four out of 26 cases in group B, and four out of 27 cases in group C, with the following occasional intakes of paracetamol or ibuprofen: three cases in group A, two in group B, and two in group C.

There was a noticeable improvement in OHRQoL after tooth bleaching, represented by significantly lower ($P < 0.05$) OHIP-14 total score values when all treatments were considered (global analysis — Table 4), with an ES of 0.1 and an SRM of 0.4 (low to moderate effect). That improvement compared to baseline was maintained up to 6 months, with an ES of 0.1 and an SRM of 0.2 (low effect). However, no significant differences ($P > 0.05$) in OHIP-14 scores were detected within or between groups, indicating that changes in OHRQoL are not related to the bleaching technique.

The percentage of cases in which the OHIP-14 total score difference was attained or surpassed the MID value of five was 18.8% after post-treatment and 13.8% at the 6-month follow-up compared to baseline values. Additionally in Table 4, are presented the scores for the seven domains of the OHIP-14 individually which assessment did not reveal any significant results ($P > 0.05$) between techniques or stages.

Discussion

The tested techniques presented bleaching efficacy with mean $\Delta E_{00}/\Delta WI_D$ above the respective AT and WAT values of 1.8 and 2.6, while the PT of 0.8 and the WPT of 0.72 were surpassed in at least 98% of treatments. Group C

Table 3 Mean and 95% IC values for ΔE_{00}, ΔWI_D, ΔSGU_{VC}, and ΔSGU_{VB} at different times with intergroup analysis. Also presented the percentages of cases, for each group, in which $\Delta E_{00}/\Delta WI_D$ surpassed the respective perceptibility (PT/WPT) and acceptability (WAT) thresholds. *Statistically significant difference ($P < 0.05$) by one-way ANOVA with Tukey post hoc

		Baseline — after bleaching 80 cases			After bleaching — 6-month follow-up 80 cases			Baseline — 6-month follow-up 61 cases		
		Group A 27 cases $n=54$	Group B 26 cases $n=52$	Group C 27 cases $n=54$	Group A 20 cases $n=40$	Group B 20 cases $n=40$	Group C 21 cases $n=42$	Group A 20 cases $n=40$	Group B 20 cases $n=40$	Group C 21 cases $n=42$
ΔE_{00}	Canines	4.0 [3.7:4.3]	4.3 [4.0:4.7]	**7.7*** **[7.0:8.3]**	0.9 [0.8:1.1]	1.2 [0.7:1.7]	**2.1*** **[1.7:2.4]**	3.7 [3.4:4.0]	4.0 [3.7:4.3]	**6.0*** **[5.3:6.7]**
	Incisors	2.6 [2.3:2.8]	2.4 [2.1:2.7]	**4.4*** **[4.0:4.8]**	1.1 [0.9:1.3]	1.0 [0.7:1.2]	**1.7*** **[1.4:2.1]**	1.9 [1.6:2.2]	2.1 [1.8:2.4]	**3.2*** **[2.7:3.7]**
ΔWI_D	Canines	11.0 [10.0:11.0]	11.8 [10.7:12.9]	**21.1*** **[19.6:23.4]**	1.3 [1.0:1.6]	1.7 [1.1:2.2]	**4.5*** **[3.6:5.3]**	10.8 [9.9:11.6]	10.8 [9.8:11.8]	**18.5*** **[16.5:20.4]**
	Incisors	5.8 [4.9:6.6]	5.7 [4.9:6.4]	**10.7*** **[9.5:12.0]**	1.4 [1.1:1.8]	1.3 [0.9:1.7]	**2.5*** **[1.9:3.1]**	7.0 [5.8:8.3]	**5.1*** **[4.3:5.9]**	8.5 [7.3:10.2]
ΔSGU_{VC}	Canines	7.5 [6.9:8.0]	6.7 [6.2:7.1]	**9.1*** **[8.6:9.5]**	2.7 [1.9:3.5]	1.6 [1.0:2.3]	2.5 [1.9:3.1]	5.1 [4.4:5.9]	5.1 [4.4:5.8]	**7.4*** **[6.7:8.2]**
	Incisors	3.6 [3.1:4.1]	**2.6*** **[2.1:3.1]**	3.1 [2.7:3.4]	**0.9*** **[0.7:1.1]**	0.3 [0.1:0.6]	0.4 [0.2:0.5]	2.8 [2.0:3.6]	2.3 [1.7:2.9]	2.7 [2.3:3.0]
ΔSGU_{VB}	Canines	4.0 [3.7:4.4]	4.2 [3.8:4.6]	**5.9*** **[5.6:6.3]**	1.5 [1.2:1.9]	**1.1*** **[0.8:1.3]**	2.0 [1.7:2.4]	2.7 [2.3:3.1]	3.4 [2.9:3.9]	**4.2*** **[3.7:4.7]**
	Incisors	3.1 [2.8:3.4]	2.6 [2.2:3.0]	**3.7*** **[3.4:4.0]**	1.4 [1.1:1.6]	0.9 [0.7:1.2]	1.0 [0.8:1.3]	1.9 [1.5:2.2]	2.1 [1.7:2.5]	**2.7*** **[2.4:3.0]**
% cases $\Delta E_{00} > PT$	Canines	100	100	100	49.5	47.2	90.5	100	100	90.5
	Incisors	98.1	98.1	100	48.4	42.8	83.3	95.2	97.2	92.9
% cases $\Delta E_{00} > AT$	Canines	98.1	98.1	100	2.6	11.1	47.6	97.4	97.2	90.5
	Incisors	72.2	75.0	96.3	2.6	8.3	35.7	88.1	88.1	83.3
% cases $\Delta WI_D > WPT$	Canines	100	100	100	67.8	69.4	95.2	100	100	100
	Incisors	98.1	98.1	100	68.4	69.4	88.1	100	100	100
% cases $\Delta WI_D > WAT$	Canines	98.1	98.1	100	13.2	25.0	71.4	100	100	95.2
	Incisors	81.5	94.2	100	15.8	13.9	40.5	86.8	88.8	92.9

presented the higher bleaching efficacy and the highest tooth color relapse at the 6-month follow-up, thus rejecting both first and second null hypotheses. Additionally, tooth bleaching with 6% HP or its CP equivalent significantly improved patients' OHRQoL, although without detectable differences between techniques, thus accepting the third and fourth null hypothesis.

To the authors' knowledge, this is the first randomized controlled trial comparing multiple different bleaching systems (both in-office and at-home) that evaluates efficacy (tooth color change) and long-term outcomes (tooth color relapse) by objective methods while evaluating patient-reported outcomes (effects in OHRQoL). Visual shade analysis was also performed since shade guides are a commonly employed method in clinical practice; however, the subjectivity of its assessment reduces accuracy and reliability, requiring the supporting use of an objective method [60].

By testing systems with similar HP concentration, the authors intended to pragmatically assess different factors on treatment outcomes, such as the application time, the delivery method, or the necessary patient's compliance. In fact, the results suggest that efficacy outcomes and treatment time efficiency depend on the clinical protocol since the group C, which presented the highest $\Delta E_{00}/\Delta WI_D/\Delta SGU$, requires approximately 30 to 40 h to attain the same bleaching effect as 2 h treatment in the group A. When applied as an in-office technique, this varnish can attain or even surpass tooth color/whitening acceptability thresholds in just 1 h, probably due to the proper soft-tissue isolation that reduces contact with crevicular fluids or the continuous evaporation of the varnish's solvent leading to a potential HP concentration increase in the tooth surface [25]. Therefore, the VivaStyle Paint On Plus (group A) has a higher efficacy in a shorter time than at-home techniques with the same HP concentration. However, further studies are required to evaluate if the product's full performance is attained with the current protocol, as increasing the number of in-office applications could potentially increase $\Delta E_{00}/\Delta WI_D/\Delta SGU$ values. A previous meta-analysis highlighted this problem stating that

Table 4 Mean, median, and 95% IC values for OHIP-14 total score and domain score at different times, divided by global and group analysis. No significant differences ($P > 0.05$) were detected between groups with Kruskal–Wallis test. *Statistically significant difference ($P < 0.05$) by Friedman test

	Baseline 80 cases $n = 80$			After bleaching 80 cases $n = 80$			6-month follow-up 61 cases $n = 61$		
OHIP-14 Total score	**Mean 2.8*** **Median 1.0** **[1.9:3.8]**			Mean 1.7 Median 0 [1.0:2.1]			Mean 2.1 Median 0 [1.3:3.0]		
	Group A 27 cases $n = 27$	Group B 26 cases $n = 26$	Group C 27 cases $n = 27$	Group A 27 cases $n = 27$	Group B 26 cases $n = 26$	Group C 27 cases $n = 27$	Group A 20 cases $n = 20$	Group B 20 cases $n = 20$	Group C 21 cases $n = 21$
	Mean 3.0 Median 2.0 [1.2:5.1]	Mean 2.4 Median 1.0 [0.9:3.5]	Mean 3.0 Median 1.0 [1.0:5.4]	Mean 1.7 Median 1.0 [1.0:3.3]	Mean 1.1 Median 0 [0.2:1.9]	Mean 1.7 Median 0 [0.3:3.1]	Mean 2.9 Median 1.0 [0.:5.1]	Mean 1.6 Median 0 [0.4:2.8]	Mean 2.0 Median 0 [0.4:3.5]
OHIP-14 functional limitation score	Mean 0.2 Median 0 [0:0.6]	Mean 0.1 Median 0 [0:0.2]	Mean 0.1 Median 0 [0:0.3]	Mean 0.4 Median 0 [0.1:0.7]	Mean 0.1 Median 0 [0:0.2]	Mean 0.1 Median 0 [0:0.3]	Mean 0.1 Median 0 [0:0.3]	Mean 0.1 Median 0 [0:0.2]	Mean 0.1 Median 0 [0:0.2]
OHIP-14 physical pain score	Mean 0.7 Median 0 [0.2:1.1]	Mean 0.6 Median 0 [0.3:0.9]	Mean 0.7 Median 0 [0.1:1.2]	Mean 0.7 Median 0 [0.3:1.1]	Mean 0.3 Median 0 [0.0:0.6]	Mean 0.3 Median 0 [0:0.6]	Mean 0.6 Median 0 [0.2:1.0]	Mean 0.4 Median 0 [0:0.9]	Mean 0.1 Median 0 [0:0.3]
OHIP-14 psychological discomfort score	Mean 1.3 Median 0 [0.5:2.1]	Mean 0.8 Median 0 [0.1:1.2]	Mean 1.2 Median 0 [0.4:2.0]	Mean 0.9 Median 0 [0.3:1.5]	Mean 0.4 Median 0 [0.1:0.8]	Mean 0.6 Median 0 [0.1:1.2]	Mean 1.3 Median 0 [0.4:2.0]	Mean 0.8 Median 0 [0.1:1.3]	Mean 1.0 Median 0 [0.2:1.7]
OHIP-14 physical disability score	Mean 0.3 Median 0 [0:0.7]	Mean 0.2 Median 0 [0:0.4]	Mean 0.3 Median 0 [0:0.6]	Mean 0.2 Median 0 [0:0.5]	Mean 0.1 Median 0 [0:0.2]	Mean 0.1 Median 0 [0:0.3]	Mean 0.1 Median 0 [0:0.3]	Mean 0.1 Median 0 [0:0.2]	Mean 0.2 Median 0 [0:0.5]
OHIP-14 psychological disability score	Mean 0.6 Median 0 [0.3:1.0]	Mean 0.4 Median 0 [0.1:0.6]	Mean 0.4 Median 0 [0.0:0.7]	Mean 0.2 Median 0 [0:0.4]	Mean 0.2 Median 0 [0:0.4]	Mean 0.3 Median 0 [0:0.5]	Mean 0.5 Median 0 [0.1:0.9]	Mean 0.2 Median 0 [0:0.4]	Mean 0.5 Median 0 [0.1:0.9]
OHIP-14 social disability score	Mean 0.4 Median 0 [0.0:0.8]	Mean 0.1 Median 1.0 [0:0.1]	Mean 0.4 Median 0 [0.0:0.8]	Mean 0.3 Median 0 [0.1:0.5]	Mean 0.1 Median 0 [0:0.3]	Mean 0.2 Median 0 [0:0.4]	Mean 0.6 Median 0 [0.2:1.0]	Mean 0.2 Median 0 [0.0:0.5]	Mean 0.3 Median 0 [0.0:0.6]
OHIP-14 handicap score	Mean 0.1 Median 0 [0:0.2]	Mean 0.1 Median 0 [0:0.1]	Mean 0.1 Median 0 [0:0.1]	Mean 0.1 Median 0 [0:0.2]	Mean 0.1 Median 0 [0:0.1]	Mean 0.1 Median 0 [0:0.1]	Mean 0.2 Median 0 [0:0.3]	Mean 0.1 Median 0 [0:0.1]	Mean 0.1 Median 0 [0:0.1]

the application time or the number of applications may be inadequate for a full HP release in some bleaching products, thus undervaluing their efficacy/effectiveness [61].

Because patients' concerns are not exclusively related to the treatment result but also the long-term outcomes, it is important to follow up on every possible case. All tested systems presented color stability up to 6 months, regardless of the percentage of tooth color relapses, since most differences were still superior to the AT thresholds compared to baseline. Additionally, only a small percentage of cases needed touch-up (between 11.9 and 16.7%), in agreement with previous studies that tested similar concentration products [9, 29–33, 36]. However, color stability values differed among techniques, and the bleaching system that attained a higher tooth color change was the same with a higher tooth color relapse — Opalescence PF (group C). This higher tooth color relapse may explain the similar whiteness results in the upper central incisors at the 6-month follow-up between groups A and C (considering group A's lower tooth color relapse values).

Patients' reports revealed improvements in OHRQoL after bleaching treatment that were maintained up to 6 months, even though that effect seems to decrease over time, as suggested by lower SRM values. This finding supports the idea that whiter and lighter tooth color may be related to patient satisfaction, consequently impacting OHRQoL, since tooth color is a major factor of an aesthetic smile and can have a psychological influence by positively changing a patient's self-esteem and social behaviors [2, 3, 34]. However, a meta-analysis concluded that the impact of tooth bleaching improvements on OHRQoL is hardly detected clinically, especially in heterogeneous populations [34]. Accordingly, our results suggest that only a small percentage of cases attained the OHIP-14 MID value, indicating that the improvements in overall OHRQoL may not be clinically relevant. Nevertheless, this could be related to the fact that the OHIP-14 MID value was established for general oral treatments and not specifically for tooth bleaching, thus not providing a reliable threshold [46].

Our results also suggest that the OHRQoL improvement is related to the bleaching treatment itself and not to any specific

technique, as significant differences in the OHIP-14 total score were detected when evaluating all cases globally. When evaluating each tested system individually, a similar effect on OHRQoL was detected despite minor adverse effects mostly related to mild and transient tooth sensitivity and gingival irritation, which were reported during the whole treatment in at-home techniques (constant low level of tooth sensitivity) and on treatment days in the in-office technique. These higher tooth sensitivity levels and some transitory oral lesion occurrences, as reported in other studies, were expected for the in-office technique due to the lower viscosity and faster HP release of the varnish, increasing the difficulty of soft tissues' isolation and tooth sensitivity during application [24, 27, 28].

As in most tooth bleaching clinical studies, limitations include participants being mostly between 20 and 30 years of age, probably due to the inclusion/exclusion criteria requiring anterior teeth free of decays/restorations and the higher demand for aesthetic treatments by younger individuals [62]. Although evidence suggests a significant relationship between the subject's age and the magnitude of the whitening response (younger subjects experience greater effects), in older populations, tooth bleaching could be effective considering the reported positive correlation between yellow hues and bleaching effects [63].

The generality of this study's results may be applied to clinical practice, although a patient-centered approach should always be considered. An in-office technique, such as the VivaStyle Paint On Plus (group A), would be suitable for faster treatments or low compliance patients, while at-home techniques could be a treatment option when it is not suitable to perform several clinical bleaching sessions. Additionally, the choice between wearing a custom (Opalescence PF — group C) or an adaptable/disposable tray (Opalescence GO — group B) could be made based on the inability to be submitted to dental impressions (e.g., vomit reflex) or difficulties in positioning the adaptable tray causing frequent displacements, as detected in our study patients' reports. Since the tested systems have their own advantages, a combined approach, where the treatment is performed in the dental office along with an at-home protocol, could be proposed to achieve a balance between tooth color change, time efficiency, and color stability. Therefore, further studies should address assistant bleaching protocols to evaluate the treatment potential of the tested bleaching systems in a combine approach.

Conclusions

All techniques presented bleaching efficacy and color stability up to the 6-month follow-up, even though a small percentage of color relapses must be expected. Tooth bleaching produces positive changes in OHRQoL, with low to moderate effects that are still detectable at a 6-month follow-up; however, these improvements are not associated with any of the tested systems.

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Declarations

Ethics approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Faculty of Dental Medicine of the University of Lisbon.

Consent to participate and consent for publication It was obtained from all individual participants included in the study an informed consent regarding study procedures/information and publishing data.

Conflict of interest The authors declare no competing interests.

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