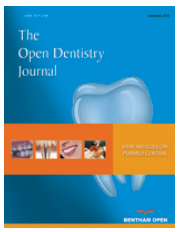

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CLINICAL TRIAL STUDY

# Evaluation of In-office Vital Tooth Whitening Combined with Different Concentrations of At-home Peroxides: A Randomized Double-blind Clinical Trial

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**Abstract:**

***Background:***

The clinical evidence relate the effect of associating the in-office and at home vital tooth whitening, describing positive effects on tooth color change and reduction of dental sensitivity.

***Objective:***

The purpose of this randomized double-blind clinical trial was to evaluate the effect on the shortened application of in-office vital tooth whitening combined with different concentrations of at-home peroxides in the final tooth color change and dental sensitivity.

***Methods:***

Randomized double-blind clinical trial with 120 participants between 18-65 years, allocated in four tooth whitening treatment groups: G1= Carbamide Peroxide 10% + Hydrogen Peroxide 40%, G2= Carbamide Peroxide 15% + Hydrogen Peroxide 40%, G3= Carbamide Peroxide 20% + Hydrogen Peroxide 40%, G4= Hydrogen Peroxide 10% + Hydrogen Peroxide 40% was conducted. Tooth color was measured at baseline and dental sensitivity and tooth color change during and after treatment.

***Results:***

No statistical significant differences were found in tooth color change (superior arch $p$= 0.183 / inferior arch $p$= 0.374), and in dental sensitivity ($p$=0.268).

***Conclusion:***

Reducing the application time of in-office whitening, combined with in-home products was effective in improving the color. All groups resulted in identical final color change and dental sensitivity.

Clinicaltrials.gov: NCT02682329 Available from: https://clinicaltrials.gov/ct2/show/NCT02682329?term=hydrogen+peroxide.

**Keywords:** Hydrogen peroxide, Carbamide peroxide, Tooth whitening, Dental sensitivity, Tooth bleaching, Dental Esthetics.

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|---|---|---|---|

## 1. INTRODUCTION

Vital Tooth Whitening (VTW) is a widely documented non-invasive technique that improves the aesthetic for discolored teeth [1 - 10]. At - home VTW with custom or prefill trays is usually done daily for several hours per week with low concentrations (10% to 20% resulting in 3.35 - 7% hydrogen peroxide) of Carbamide Peroxide (CP) [11 - 13]. The 10% CP is considered as the "gold standard" for VTW, since it presents great results with lower risk and intensity of Dental Sensitivity (DS) for the patients [3, 7, 13 - 17]. Despite its advantages, some patients request quicker results, therefore in-office, VTW using higher concentrations (20 -40%) of Hydrogen Peroxide (HP) is an alternative [18 - 20]. Both techniques have shown

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favorable effectiveness in color changes [1, 3, 5, 9, 11, 13, 14, 19 - 23].

In order to overcome the drawbacks of each procedure, the combination of both methods has been widely accepted, resulting in achieving fast effects with less gingiva irritation and DS [8, 12, 22, 24]. However, Machado *et al*. [22], found that the combined technique produced greater DS and the same whitening results when compared to the at-home technique. Vaez *et al*. [19], concluded that the combined technique reduced the time necessary to obtain satisfactory tooth color compared with at-home bleaching, but increased the risk and level of DS.

Longer contact time and higher peroxide concentrations provide faster result, though a medium to severe intensity of DS has been reported [2, 4, 11, 21, 23, 25]. To decrease DS in at-office protocols, it has been suggested that a single application of the VTW gel is applied, since the amount of product that reaches the pulp might be reduced, although Reis *et al*. [18], showed that one 45 minutes application reduces the whitening speed and increases the DS intensity, compared to 3-15 minutes protocol. In order to decrease the interaction with high Hydrogen Peroxide concentration, Rodriguez *et al*. [4], evaluated the combined technique with two in-office sessions, showing that both protocols result in acceptable color and same DS, in this order Kose *et al*. [10], found that a single 15 minutes session produced less DS but reduced the whitening effect. Roderjam *et al*. [21], concluded that calcium-containing gel could cause less pulp damage and DS. Obtaining acceptable results in terms of satisfactory color modification with none or minimal DS has been the main objective of clinical researchers, this is why continuing modifications in the VTW protocols is still proposed.

To the best of authors' knowledge, no clinical study has evaluated the whitening effect of the combined technique with shortened application. Therefore, the purpose of this randomized double-blind clinical trial was to evaluate the effect on color change and DS when decreasing the application time of in-office VTW combined with different concentrations of at-home products.

## 2. MATERIALS AND METHODS

This clinical trial was approved by UNIBE's Ethics Committee (CEI) No. CEI2013-07 and The National Committee for Health Bioethics (CONABIOS) No.024-2013 [26]. The clinical trials identifier is: NCT02682329 [27]. This report follows the protocol established by CONSORT Statement. The study design was a randomized double-blind clinical trial (Fig. **1**).

### 2.1. Eligibility Criteria

An open call was started to recruit the sample, volunteers requiring vital tooth whitening were selected for this study. The clinical trial was conducted at the school of dentistry of Universidad Iberoamericana (Santo Domingo, Dominican Republic) from September 2013- February 2014.

A total of 120 participants between ages 18 to 45 were recruited at the UNIBE'S dental clinics and after signing the informed consent, a medical and the dental record were completed. After a dental prophylaxis and clinical examination, it was determined if the subject was able to participate in the study according to the exclusion criteria defined: patients with caries, restoration, veneers of full crowns or endodontic treatment, severe stains, enamel hypoplasia, severe internal tooth discoloration, gingival recession, spontaneous tooth pain, previous bleaching procedure, use of orthodontics appliances up to the second premolar of both dental arches. Also, patients with bruxism habits, taking analgesic or anti-inflammatory drugs, smokers, and pregnant or lactating applicants were excluded.

### 2.2. Randomization

Four groups of treatment were defined, the randomization occurred through a card color system for the codification of the different peroxide concentrations of bleaching syringes and to be able to assign the participant into groups, only the principal Investigator was aware of system details. Details of the composition, mode of application and brands of the whitening products are described in Table **1**. The participants were randomly assigned into 4 experimental groups: G1= Carbamide Peroxide 10% (CP10%) + Hydrogen Peroxide 40% (HP40%) G2= Carbamide Peroxide 15% (CP15%) + Hydrogen Peroxide 40% (HP40%), G3= Carbamide Peroxide 20% (CP20%) + Hydrogen Peroxide 40% (HP40%), G4= Hydrogen Peroxide 10% (HP10%) + Hydrogen Peroxide 40% (HP40%) (Table **2**).

### 2.3. Study Intervention

#### *2.3.1. In-office VTW Procedure*

All patients included in the study were subjected to an initial in-office VTW with 40% HP (Opalescense Xtra Boost Ultradent, USA) without light activation as recommended by the manufacturer. The VTW procedure was performed up to the second premolar of both dental arches (first molar could be included in case of absence of the second premolars). A light-cure resin dam was applied to the gingival tissue to isolate and protect it. The in-office VTW was applied for 20 minutes single application. The manufacturer's recommendation is 45 minutes application in three consecutive 15-minutes intervals. After finishing the process; the teeth were rinsed with copious water. The in-office VTW was performed in two sessions, with an interval of 8 days between them, during which time home bleaching was done.

#### *2.3.2. At-home VTW Procedure*

For groups 1, 2 and 3 alginate impressions (Tropicalgin - Zhermark) of both arches were made. The stone molds were produced to fabricate the whitening trays with reservoirs. The patients were instructed to place a small drop of the gel into each tooth of the tray; then after insertion, the excess of gel must be wiped away from the gingiva with a quick tip. Group 4 used prefabricated trays. The patients were advised to use the in-home VTW daily for 1 hour according to the allocation: group 1 for 7 days; group 2 for 5 days; group 3 and 4 for 2 days.

**Table 1. Details of the brand, composition and mode of application according to the manufacturer.**

| Material | Brand | Composition | Mode of Application |
|---|---|---|---|
| Opalescence® Boost (HP40%) | (Ultradent Products Inc, South Jordan, US) | 40% hydrogen peroxide, chemical activator, 1.1% fluoride, 3% potassium nitrate. | In-office bleaching agent. Three applications of 20 minutes. Remove it with a soft pellet; rinse twice with copious water. Repeat the procedure in 2 other applications with 3-day interval between each one. |
| Opalescence® 10% (CP10%) | (Ultradent Products Inc, South Jordan, US) | 10% carbamide peroxide, Carbopol, glycerin, flavoring. | To the patient: Express one continuous bead of gel approximately halfway up the facial side of your tray. Place the tray over your teeth and gently press. Wear for 8-10 hours, or overnight. After whitening, remove the tray and use a soft toothbrush, or your finger, to clean any excess gel off your teeth. |
| Opalescence® 15% (CP15%) | (Ultradent Products Inc, South Jordan, US) | 15% carbamide peroxide, Carbopol, glycerin, flavoring. | To the patient: Express one continuous bead of gel approximately halfway up the facial side of your tray. Place the tray over your teeth and gently press. Wear for 6-8 hours. After whitening, remove the tray and use a soft toothbrush, or your finger, to clean any excess gel off your teeth. |
| Opalescence® 20% (CP20%) | (Ultradent Products Inc, South Jordan, US) | 20% carbamide peroxide, Carbopol, glycerin, flavoring. | To the patient: Express one continuous bead of gel approximately halfway up the facial side of your tray. Place the tray over your teeth and gently press. Wear for 2-4 hours. After whitening, remove the tray and use a soft toothbrush, or your finger, to clean any excess gel off your teeth. |
| Opalescence® TresWhite Supreme (HP10%) | (Ultradent Products Inc, South Jordan, US) | 10% Hydrogen peroxide, glycerin, flavoring | Remove the tray and align it correctly over your teeth. Gently suck on the tray to create suction, so that the tray will adhere to your teeth. Detach the external part of the tray. Tap gently on the remaining part of the tray to ensure that it is securely attached to your teeth. Leave it in place for 30 to 60 minutes. Remove the tray from your mouth and cleanse your teeth of the excess gel by brushing as necessary. |

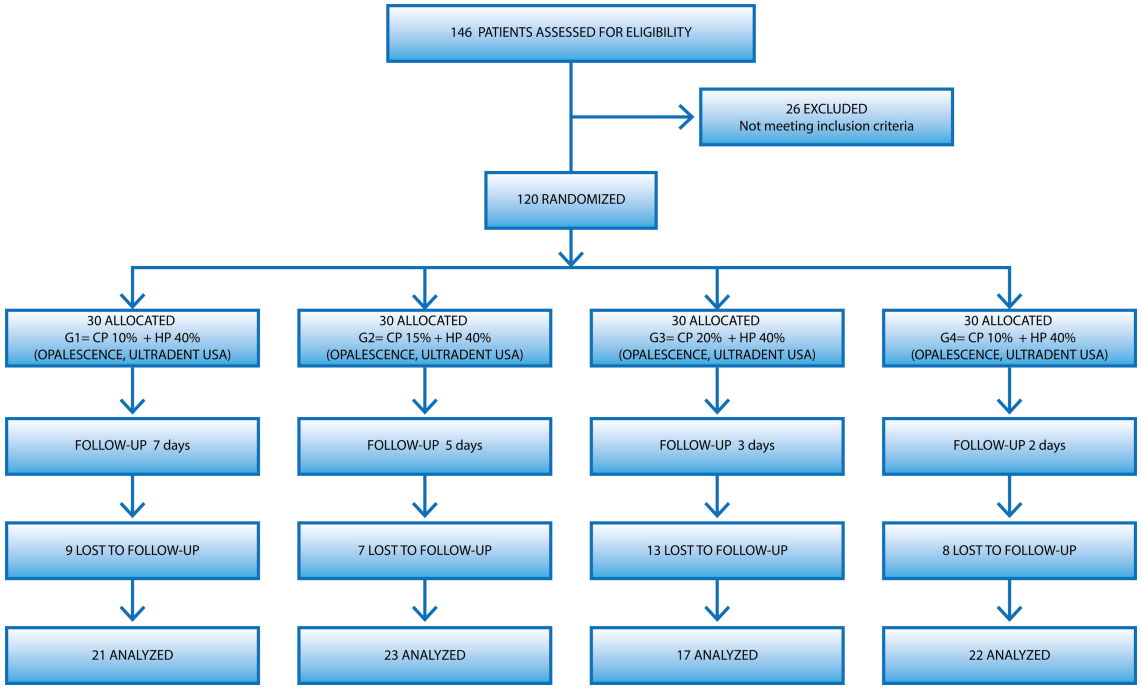


**Fig. (1).** Consort flow diagram of the clinical trial.

Analgesic, anti-inflammatory or desensitizing gels were indicated to the patient with moderate and severe tooth sensitivity [4].

### *2.3.3. Visual Analysis of Color Change*

The visual analysis of color change was recorded for each volunteer in four intervals: 1. At baseline, 2. Immediately after in-office session, 3. After the conclusion of at-home treatment and 4. Final color tooth measurement, using a shade guide (Vita Classical, Vita Zahn Fabric) organized by scores from B1 (1) to C4 (16). The middle third of the canines of both dental arcades were analyzed for the degree of color change. Two calibrated examiners performed the evaluations; the final color was determined based on a consensus of both.

### *2.3.4. Dental Sensitivity Analysis*

DS was analyzed after the at-office and at-home VTW treatment. The visual analogue scale method was used, with a scale 0 to 3, with 0 indicating no sensitivity, 1low sensitivity, 2 medium sensitivity and 3 indicating severe sensitivity.

**Table 2. Experimental groups.**

| Group | Products | Use |
|---|---|---|
| 1 | CP 10%/ HP40% | 6 hours/ 7 days |
| 2 | CP 15% /HP40% | 6 hours/ 5 days |
| 3 | CP 20% /HP40% | 6 hours /3 days |
| 4 | HP 10% /HP40% | 1 hour / 2 days |

### *2.3.5. Statistical Analysis*

The data collected from 83 patients was registered. The mean and standard deviation were calculated for each group at each evaluation intervals. The two- way ANOVA and Tukey for pairwise comparison ($p<.05$) were used. The mean of color change were analyzed using one-way analysis of variance (ANOVA) to evaluate the color change between groups at each interval. The means of dental sensitivity were compared using the One- way ANOVA and Tukey test ($p<0.05$) for each whitening protocol. All results were analyzed using the SPSS version (23) (SPSS inc, Chicago, IL, USA).

## 3. RESULTS

A total of 120 patients were included in this clinical study, where 83 completed the whitening protocol and attended recalls appointment, 37 volunteers did not complete the treatment or missed appointments for evaluation.

The baseline tooth color in the superior arch was 4.76 +/-3.53 and 6.89 +/- 2.78 in the inferior arch. The mean color change results for each group are described in Table **3** and **4**. Analysis of variance (ANOVA) and HSD Tukey test detected that there was no statistical significance for the color change in the superior/ inferior arc for de 4 experimental groups ($p$= 0.183/ $p$=0.374). All in-office combined with different in-home gels were effective for color change for vital tooth whitening (Tables **4**-**5**). No statistically significant differences were found in tooth color change between subjects, $p$= 0.065 and within subjects, $p$= 0.187

The final DS mean of each group are described in Table **6**. No statistically significant differences were found in dental sensitivity between subjects, $p$=0.268 (Table **7**).

**Table 3. Mean values of color change superior arch in each intervention.**

| - | Groups | - | - | - |
|---|---|---|---|---|
| **Periods** | **1** | **2** | **3** | **4** |
| Baseline | 7.33+/-1.82 | 6.70+/-3.09 | 6.76+/-2.68 | 5.50+/-3.3 |
| After at-office session | 4.29+/- 2.15 | 3.91+/-2.37 | 4.12+/-2.06 | 3.14+/-1.75 |
| After at-home session | 4.14+/-2.52 | 3.17+/-1.72 | 3.76+/-2.92 | 3.50+/-2.94 |
| After final at-office session | 2.62+/-1.72 | 2.04+/-1.43 | 2.76+/-2.86 | 1.77+/-1.34 |

## 4. DISCUSSION

The whitening effect is related to the concentration and application time [10, 13], all the techniques investigated in this randomized double-blind clinical trial showed significant color change with no statistical differences between the groups, regardless of in-home concentration, from 10 to 20% and application protocol, from 2 to 7 days. This has an important clinical implication: reducing the in-office time to half, from 40 minutes, indicated by the manufacturer, to 20 minutes in two sessions, combined with at-home products for just 2 days (group 4) could be effective in better tooth whitening results.

**Table 4. Mean values of color change inferior arch in each intervention.**

| - | Groups | - | - | - |
|---|---|---|---|---|
| **Periods** | **1** | **2** | **3** | **4** |
| Baseline | 7.36+/-2.15 | 7.14+/-3.04 | 7.59+/-2.76 | 5.57+/-2.84 |
| After at-office session | 5.15+/-2.27 | 4.05+/-2.67 | 5.00+/-3.5 | 4.48+/-3.82 |
| After at-home session | 4.64+/-2.57 | 4.14+/-2.45 | 4.12+/-1.93 | 3.62+/-2.52 |
| After final at-office session | 2.54+/-1.53 | 2.19+/-1.40 | 3.00+/-2.78 | 2.33+/-1.85 |

**Table 5. Total mean values of color change inferior arch.**

| HSD Tukey | Group | Patients | Mean Color Change |
|---|---|---|---|
| - | Group 1 | 22 | 3.48 |
| | Group 2 | 23 | 3.96 |
| | Group 3 | 17 | 4.35 |
| | Group 4 | 21 | 4.60 |
| | Sig. | | 0.183 |

**Table 6. Total mean values of color change inferior arch.**

| HSD Tukey | Group | Patients | Mean Color Change |
|---|---|---|---|
| - | Group 1 | 21 | 4.00 |
| | Group 2 | 23 | 4.38 |
| | Group 3 | 17 | 4.93 |
| | Group 4 | 22 | 4.94 |
| | Sig. | - | 0.374 |

**Table 7. Mean values of dental sensitivity.**

| Group | Mean |
|---|---|
| Group 1 | 0.44+/-0.77 |
| Group 2 | 0.96+/-1.37 |
| Group 3 | 0.48+/-0.71 |
| Group 4 | 0.73+/-1.19 |

Long chair-time, usually 40 - 45 minutes in two or three different appointments and high risk of TS are most common complains about in-office VTW [2, 10, 13]. The main concern regarding in-home whitening is the longer time required to obtain a satisfactory color. Two combined protocol have been suggested, a whitening treatment in a single 40 minutes in-office session as a jump-start for the initial effect and shortening the time required for at-home procedure [19]. Rodriguez *et al*. [4], concluded that the combined protocol using a tray for 1week after the in-office VTW could increase the DS when compared to two in-office sessions.

In this study, group 4 used in-home HP 10% bleaching with a prefabricated tray for just 2 days reporting the same

results compared with the other combinations evaluated. This also has a significant clinical inference: favors the clinician's preference to simplification: This product requires no impression, plaster cats or costume made tray, reducing the treatment time. Carlos *et al*. [17], found no significant differences among the acceptance of prefill and custom-made trays. Also, aggressive bleaching protocols can cause pulp damage resulting in a rebound effect of the bleached teeth due to the production of reactional dentin [4].

The DS, a common side effect of whitening treatments, is the principal concern related to this procedure reported by patients, especially in-office treatments [2, 16, 28]. The hydrogen peroxide has a rapid diffusion into enamel prism due to its low molecular mass reaching the pulp chamber through the dentinal tubules. Although the majority of people are able to tolerate tooth whitening, sensitivity is a major problem. In this study, there was no statistical difference in sensitivity between the groups ($p$=0.268). Basting *et al*. [3], found that 13.8% participants experienced extreme sensitivity that forces them to quit the study, also Briso *et al*. [15], reported spontaneous low to moderate DS during all treatment periods, equal to the findings in this study.

Vaez *et al*. [19], found a greater risk of DS with the combined protocol compared with in-home techniques with 10% carbamide peroxide. Kose *et al*. [10], suggested that a multiple appointment with a single 15 minutes applications can reduce the pulp tissue damage with satisfactory results. Moghadam *et al*. [29], founded no differences in DS between in-office and in-home VTW techniques. Patients with darker teeth and those who used in-home VTW presented lower intensity and risk DS [23].

The method used to assess the color change in this study was the Vital Classical shade scale, as other clinical trials [3, 11, 18, 22, 28] frequently used to show the beginning and final color to the patient in dental office [17]. Two trained examiners measured the color after each session protocol was blinded to the experimental conditions. Despite the subjectivity of visual assessment, this method is easy, fast, and satisfactory with good reliability [18, 22].

In recent studies, the impact on the quality of life and the patient's level of satisfaction related to the color of their teeth before and after the bleaching treatment has been considered [9, 11, 14, 16, 19]. In the present study, the combination of an initial 20 minutes in-office therapy with different in-home protocol and a final 20 minutes whitening showed that the color change process was gradual, the initial color was between A3 - A3.5 decreasing to a final color between A1 to B1, reducing the number of days and application time, indicating that the participants were satisfied with the results. Rezende *et al*. [23], explained that regardless of the VTW technique used by the clinician, the baseline color showed a significant effect on overall whitening efficacy, especially in younger patients or with darker teeth.

The concentration agent and the bleaching technique are one of the principal factors to be considered in the effectiveness of the whitening procedure. Also Torres *et al*. [1], exposed that the efficacy of VTW is directly proportional to the pH, additionally the application time, safety, side effects evolved and patient's preferences must be taken into consideration [3]. The outcomes of this study showed that reducing in half the application time of in-office bleaching combined with at-home products results in positive VTW color changes, however further studies considering the patients' level of satisfaction could increase the evidence. Another limitation of this study was that final color was evaluated immediately after the second VTW application; Correa *et al*. [28], suggest longer periods of follow-up to allow color stabilization because teeth appear whiter immediately after the VTW procedure due to dehydration and demineralization caused by the acidity of the agent [4].

## CONCLUSION

Within the limitation of this study, it was determined that the reduction in the application time of in-office whitening with different at-home products was effective in color change for VTW, the result was the same for all groups. As for the matter of post-treatment sensitivity, all the VTW combinations were identical.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This clinical trial was approved by UNIBE's Ethics Committee (CEI) No. CEI2013-07 and The National Committee for Health Bioethics (CONABIOS) No.024-2013.

## HUMAN AND ANIMAL RIGHTS

No Animals were used in this research. All human research procedures were followed in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

## CONSENT FOR PUBLICATION

The participant provided written informed consent.

## STANDARDS OF REPORTING

This report follows the protocol established by CONSORT Statement.

## AVAILABILITY OF DATA AND MATERIALS

The authors confirm that the data supporting the findings of this study are available within the article.

## FUNDING

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## CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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