RESEARCH ARTICLE

Evaluation of post-bleaching hypersensitivity using desensitizing agent before and /or after in-office bleaching: A randomized clinical trial. [version 1; peer review: 1 approved with reservations, 1 not approved]

Silvia Sabry Tawfik ^{1,2}, Mohamed Adel Ezzat Khairy², Maha Abd Elsalam ElBaz², Maha Ebrahim Mohamed El korashy¹

¹Conservative Department, Faculty of Dentistry, Fayoum University, Fayoum, Egypt

²Conservative Dentistry, Faculty of Dentistry, Cairo University, Cairo, Egypt

V1 First published: 16 Oct 2019, 8:1762
<https://doi.org/10.12688/f1000research.20841.1>
 Latest published: 16 Oct 2019, 8:1762
<https://doi.org/10.12688/f1000research.20841.1>

Abstract

Background: Dental bleaching has become one of the most demanded aesthetic procedures as it is very simple and gives fast results that satisfy the patient's wishes. However, unfortunately, it has the annoying side effect of tooth sensitivity. This clinical trial was designed to evaluate the efficacy of using a desensitizing agent, which was applied during in-office bleaching with 30% HP (hydrogen peroxide).

Methods: 36 participants were divided into four groups (N = 9). According to the intended intervention as follows: Group I:—Application of Relief @Amorphous Calcium Phosphate (ACP) before in-office bleaching; Group II—Application of Relief @ACP before and after in-office bleaching; Group III—Application of Relief @ACP after in-office bleaching; and Group IV: placebo was applied before and after in-office bleaching. Then, three hydrogen peroxide bleaching applications for a total of 45 minutes were performed. The primary outcome variable was hypersensitivity, assessed with (VAS) scale immediately and 24h, 1 week and 1 month after the procedure; while the secondary outcome was teeth shade assessed using the VITAPAN @ classical shade guide.

Results: Statistical analysis was done using Kolmogorov-Smirnov, Shapiro-Wilk tests, Kruskal-Wallis test and Dunn's test. Immediately after bleaching, there was statistically significant distinction in the median pain score between the groups. After 1 day, the ACP gel before and after bleaching group showed the lowest median score, while, the control group confirmed the highest median score. After 2 days, no statistically sizable difference was observed between all groups. The group receiving ACP gel before and after showed the

Open Peer Review

Approval Status

	1	2
version 1		
16 Oct 2019	view	view

1. **Cristian Bersezio** , University of Chile, Santiago, Chile

2. **Eduardo Fernández** , University of Chile, Santiago, Chile

Any reports and responses or comments on the article can be found at the end of the article.

highest change in median of classical shade guide scores while, (ACP gel after) and control group; showed the lowest change.

Conclusion: The application of the desensitizing agent prior to and after in-office bleaching was successful in lowering post-bleaching hypersensitivity.

Trail Registration: Clinical trial.gov [NCT02942082](#) 21/10/2016

Keywords

Tooth bleaching, Hydrogen peroxide, hyper-sensitivity, Randomized clinical trial, in-office bleaching, VAS, desensitizing agent, ACP

This article is included in the [All trials matter](#) collection.

Corresponding authors: Silvia Sabry Tawfik (sst11@fayoum.edu.eg), Mohamed Adel Ezzat Khairy (madelkhairy@yahoo.com), Maha Abd Elsalam ElBaz (mahaaelbaz@yahoo.com), Maha Ebrahim Mohamed El korashy (dr_mahakorashy@yahoo.com)

Author roles: **Sabry Tawfik S:** Conceptualization, Data Curation, Funding Acquisition, Investigation, Methodology, Project Administration, Writing – Original Draft Preparation, Writing – Review & Editing; **Khairy MAE:** Investigation, Methodology, Supervision, Writing – Review & Editing; **ElBaz MAE:** Investigation, Supervision, Writing – Review & Editing; **El korashy MEM:** Supervision, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

Copyright: © 2019 Sabry Tawfik S *et al.* This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Sabry Tawfik S, Khairy MAE, ElBaz MAE and El korashy MEM. **Evaluation of post-bleaching hypersensitivity using desensitizing agent before and /or after in-office bleaching: A randomized clinical trial. [version 1; peer review: 1 approved with reservations, 1 not approved]** F1000Research 2019, 8:1762 <https://doi.org/10.12688/f1000research.20841.1>

First published: 16 Oct 2019, 8:1762 <https://doi.org/10.12688/f1000research.20841.1>

Introduction

In-office bleaching permits close professional control, prevents material ingestion, reduces the total treatment time, and has the potential for quick results, improving patient satisfaction¹. Be that as it may, tooth sensitivity (TS) is the most common side-effect of dental bleaching. It has been hypothesized that tooth sensitivity resulting from tooth bleaching occurs because peroxide penetrates the tooth structure and directly activates a neuronal receptor and not because of hydrodynamic effects. In addition, alteration caused by bleaching agents on the morphological enamel surface as increased surface porosity, depressions and superficial irregularities^{2,3}.

For this reason, a desensitizing agent is used to decrease the tooth sensitivity that patients experience. The mechanism of action of potassium nitrate remains unknown. This acts by diminishing the excitability of the intra-dental nerve endings and blocking the dentinal tubules⁴. Potassium nitrate and sodium fluoride are broadly used as desensitizing agents to treat tooth sensitivity. Potassium ions cause the depolarization of the sensory nerve⁵, and fluoride treats tooth sensitivity, probably by blocking uncovered dentinal tubules or decreasing the liquid stream into the mesh and blocking the transmission of improvements⁶. Of late, bioactive materials such as ACP (amorphous calcium phosphate) and CCP-ACP (casein phosphopeptide and amorphous calcium phosphate) as desensitizers and re-mineralizing specialists have been utilized for this purpose; however, there is only limited research in this area⁷. The objective of this randomized clinical trial is to assess whether the use of a desensitizing agent will diminish the tooth sensitivity induced by dental bleaching.

Methods

Research ethical approval and consent

The protocol and the informed consent template were reviewed and accepted by the Ethics committee of Scientific Research at the Faculty of Dentistry, Cairo University on October 2016 (Approval number 161038 on 24 October 2016). All participants provided written informed consent regarding all of the trial's procedural steps and the publication of the trial results and photos. The trial has been registered on clinical-trials.gov (NCT02942082) on 21 October 2016.

Study design

This was a randomized clinical trial with an equal allocation ratio (1:1:1:1). This article was prepared following the protocol established by the consolidation standards of reporting trials, statement 2010. The trial was started in November 2017 and it was completed in November 2018.

Participants

All participants were recruited from the outpatient clinic of the Conservative Department at Cairo University who attended seeking tooth whitening. In total, 36 (6 male and 30 female) adult patients took part in this trial subsequent to satisfying all inclusion criteria. Telephone numbers and addresses of all subjects in the study were recorded as part of the signed consent.

All subjects received a phone call at the time of the pre-determined follow-up dates. Patients were given a brief explanation about the investigations those who agreed to participate signed an informed consent. The in-office bleaching was performed in a single visit.

Eligibility criteria

Inclusion criteria

To be included in this trial, participants needed to be aged between 18 and 40 years old, have good oral health with no periodontal disease and have six upper anterior teeth that are free from either caries or restoration with no sign of spontaneous pain.

Exclusion criteria

Participants with anterior restorations and carious lesions in their upper labial surfaces were not included in this trial. Additionally, participants suffering from recession and cracks, those taking analgesics, and those with bruxism habits were also not enrolled in this trial. Finally, pregnant women and lactating mothers were also excluded.

Sample size

Sample size calculation was performed using the **G*Power** program version 3.1.9.2 (University of Düsseldorf, Düsseldorf, Germany). Based on post-bleaching hypersensitivity results from previous studies^{8,9}, a sample size of 36 patients was calculated. A sample of 24 patients was enough for the detection of an effect size 0.4, with a power of 85%, and a 5% significance level. The number was increased to 29 to address non-parametric variables in order to increase the reliability of the results, and again increased to 36 for loss to follow up.

Randomization and allocation concealment

Using a free online website (<http://www.random.org/>), a sequence generation for patient numbers was created. Each participant chose a number from successively numbered obscure envelopes. They were then allocated into one of the set-ups using a randomization table formed of four columns, and each column contained numbers from one to nine. The table was kept with the senior supervisor (MA) who generated the allocation sequence and he was responsible for ensuring proper randomization and allocation concealment.

Study intervention

One operator performed the bleaching procedures for all participants (SS).

First visit

After taking a medical and dental history using medical and dental health charts see (extended data¹⁰), patients were given a concise clarification regarding the examinations. A prophylaxis paste and a low-speed brush for teeth cleaning were used a day prior to bleaching. Utilizing a visual analogue scale (VAS, see extended data¹⁰), every member set a mark that represents their level of pain on a scale from 0–10. VAS scores were assessed for each patient by measuring the distance in cm from the anchor word (0 cm) to the mark.

Second visit

In-office bleaching was done using Dash™ whitening gel syringe 30% hydrogen peroxide (Discus dental, Culver City, 91761 USA) batch number DSE 1001, for three sessions each 15 minutes.

In-office bleaching procedures. After patient lip lubrication, the operator placed a cheek retractor and a bite block into the patients mouth (Figure 1). Isolation using cotton rolls was performed, and a liquid barrier material, Liquidam™ barrier syringe catalogue number 99-905-26, was applied to cover the tissues. The applied Liquidam was cured for 10 seconds. Then, according to the group specification, the following were performed: Group I: a desensitizing agent Relief® ACP oral care gel syringe (Discus Dental, Culver City, 91761 USA) batch number DSE 1001 which according to the manufacture, contains 5% potassium nitrate; 0.22% sodium fluoride and 0.75% amorphous calcium phosphate (ACP) was applied on the teeth before dental bleaching; Group II: the Relief® ACP was applied before and after bleaching procedures; Group III: Relief ACP was applied after bleaching; and Group IV: glycerin liquid (Human Care International, Egypt, Batch No. SP8P) was applied before and after bleaching procedures. Dash™ whitening gel syringe 30% hydrogen peroxide (Discus dental, Culver City, 91761 USA) batch number DSE 1001 was applied to the facial side of teeth (1–2 mm thick), and the gel was left on the teeth for 15 minutes for a total of three cycles (Figure 2). After each cycle, the gel was removed with surgical suction tip or wiped with gauze. Again, the desensitizing agent Relief® ACP Oral Care Gel or glycerin was applied on the labial surfaces of teeth according to the group specification. For Group II, Group III, and

Figure 1. Cheek retractor and bite block placement.

Figure 2. Dash™ whitening gel application.

Group IV, glycerin was applied before and after in-office bleaching. Post-operative instructions were given to the participants; for the next two days, they were asked to avoid pigmented consumption, such as tea and cola, and to avoid using toothpaste with desensitizing agents.

Outcomes evaluation

Primary Outcome

Post-bleaching hypersensitivity. Post-bleaching hypersensitivity was assessed using a VAS scale, immediately and 24 hours, one week and one month after the bleaching procedure. VAS was used by the patients from the second day after bleaching on a daily basis to record tooth sensitivity between the schedule of the subsequent evaluations, and patients were asked to bring this pain diary at every point of assessment. The assistant supervisor (ME) kept in contact with the participants by phone to remind them and to ensure accurate adherence to instructions. VAS scores were assessed for each patient by measuring the distance in cm from the anchor word (0 cm) to the mark. The blinded assessor collected the data of evaluation in a printed assessor chart (extended data¹⁰).

Secondary Outcome

Color evaluation. The blinded assessor recorded the shade of each participant's teeth at baseline and at the recall appointments (after 24 hours, 1 week and 6 months). The measurement area of interest for shade matching was the middle third of the facial surface of maxillary anterior teeth. 16 tabs of the shade guide (The VITAPAN® classical shade guide (Vita Zahnfabrik, Badsä ckingen, Germany) were arranged from highest (B1) to lowest (C4) value. These values were converted into numerical codes using a conversion table (Table 1) (Borges *et al.*, 2012).

Table 1. Tab arrangement and numeric order for Vitapan® Classical shade guide.

B1	A1	B2	D2	A2	C1	C2	D4	A3	D3	B3	A3.5	B4	C3	A4	C4
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16

Blinding

This was a double-blind clinical trial in which the participants and assessors were unaware of the type of the desensitizer used (relief® ACP oral care gel or a placebo) and were not aware of which group they were in. However, for clinical purposes, the operator was not blind, as both materials used had the same color but different consistencies; thus, it was impossible to blind the operator. The assessor collected the data from evaluations in a printed assessor chart (see extended data¹⁰).

Statistical methods

In this study, data analysis was performed using IBM SPSS statistical for Windows, Version 23.0 Armonk, NY:IBM Corp. Non-normal (non-parametric) data were represented as the median and Inter-quartile Ranges (IQR). For comparison between the four groups, a Kruskal–Wallis test was used. Friedman's test was used to study changes over time within each group. For pairwise comparison, Dunn's test and Bonferroni's test were used. Quantitative data were represented in terms of frequencies and percentages, and significance was set at $P \leq 0.05$.

Results

In this study, 36 (6 male and 30 female) adult patients took part in this trial (see underlying data). A patient flow chart is available as part of the Reporting guidelines¹⁰.

Patient ages ranged between 18–40 years old; their mean ages were 32.4 ± 4.3 , 32.1 ± 4.4 , 33.1 ± 4.8 and 32.1 ± 5.3 for the ACP gel before bleaching group, ACP gel before and after bleaching group, ACP gel after bleaching and the control group, respectively, with no statistically significant difference regarding mean age values (P -value = 0.965) between all groups.

Regarding patient gender, the ACP gel before bleaching group included two males (22.2%) and seven females (77.8%), while the ACP gel before and after bleaching group included one male (11.1%) and eight females (88.9%), the ACP gel after bleaching group included one male (11.1%) and eight females (88.9%) and the control group, glycerin before and after bleaching, included two males (22.2%) and seven females (77.8%). Regarding gender distribution, no significant difference ($p = 1.000$) was found. (Table 2)

A comparison of the VAS scores is shown in Table 3 and Figure 3. Before bleaching, all cases in the study groups showed no pain (P -value = 1.000, Effect size = 0.000). A significant difference was shown in all groups immediately after bleaching (P -value < 0.001, Effect size = 3.149). Regarding pairwise comparison between the groups, the ACP gel after bleaching and glycerin before and after bleaching groups showed the highest median pain score of 5 (4–6.5) and 5 (5–7), respectively, with a non-statistically significant difference between both groups and that of the ACP gel before bleaching group, which was 4 (3.5–4.5). The ACP gel before and after bleaching group showed the lowest median pain score of 3 (0–4), with a non-statistically significant difference from the ACP gel before bleaching group, which was 5 (5–7), and a statistically significantly lower median pain score than the ACP gel after bleaching and glycerin applied before and after bleaching groups, at 5 (4–6.5) and 5 (5–7), respectively. After 1 day, a significant difference was revealed between the groups (P -value < 0.001, Effect size = 3.367). Pairwise comparison between the groups revealed that the glycerin before and after bleaching group showed the highest median pain score of 3 (2–3.5), with a non-statistically significant difference from the ACP gel after bleaching group, which was 2 (1–2.5). The ACP gel before and after bleaching group showed the lowest median pain score 0 (0–1), with a non-statistically significant difference from the ACP gel before bleaching group, at 1 (0.5–1.5), and a statistically significantly lower median pain score than the ACP gel after bleaching and glycerin applied before and after groups, at 2 (1–2.5) and 3 (2–3.5), respectively. On day 2 after bleaching, a statistically significant difference was shown (P -value = 0.099, Effect size = 1.046). For days 3, 4, 5, 6 and 7, and even after 1 month, all cases of the four groups showed no pain.

Changes in hypersensitivity scores after bleaching within each group

Change over time in VAS score within each group

Results for changes in hypersensitivity are presented in Table 4 and Figure 4. In the ACP gel before bleaching group, the median pain score values changed statistically significantly over time (P -value < 0.001, Effect size = 0.437). The pair-wise comparison showed a statistically significant rise in the 0 median pain results instantly after bleaching followed by a statistically significant reduction in pain results after 1 day. Days 1 to 2 did not alter pain statistically significantly. No statistically significant change was

Table 2. Demographic data shown as mean, standard deviation (SD), frequencies (n), percentages and results of one-way ANOVA test, Fisher's Exact of different groups.

Variables		ACP gel before bleaching (n = 9)		ACP gel before & after bleaching (n = 9)		ACP gel after bleaching (n = 9)		Glycerin before & after bleaching (n = 9)		P-value
Character		No.	%	No.	%	No.	%	No.	%	
Age(By years): Mean $\pm$ SD		32	4.3%	32.1	4.4%	33.1	4.8%	32.1	5.3%	0.965
Gender	Males	2	22.2%	1	11.1%	1	11.1%	2	22.2%	1.000
	Females	7	77.8%	8	88.9%	8	88.9%	7	77.8%	

*, Significant at $P \leq 0.05$

ACP - Amorphous calcium phosphate

Table 3. Results of Kruskal –Wallis test for sensitivity score comparison between the groups.

Time	ACP gel before bleaching (n = 9)	ACP gel before & after bleaching (n = 9)	ACP gel after bleaching (n = 9)	Glycerin before & after bleaching (n = 9)	P-value	Effect size (Eta Squared)
Before bleaching	0 (0 – 0)	0 (0 – 0)	0 (0 – 0)	0 (0 – 0)	1.000	0.000
Immediately after bleaching	4 (3.5 – 4.5) AB	3 (0 – 4) B	5 (4 – 6.5) A	5 (5 – 7) A	<0.001*	3.149
Day 1	1 (0.5 – 1.5) B	0 (0 – 1) B	2 (1 – 2.5) A	3 (2 – 3.5) A	<0.001*	3.367
Day 2	0 (0 – 0.5)	0 (0 – 0)	0 (0 – 0)	0 (0 – 1)	0.099	1.046
Day 3	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	1.000	0.000
Day 4	0 (0-0)	0 (0-0)	0 (0-0)	0 (0 – 0)	1.000	0.000
Day 5	0 (0-0)	0 (0-0)	0 (0-0)	0 (0 – 0)	1.000	0.000
Day 6	0 (0-0)	0 (0-0)	0 (0-0)	0 (0 – 0)	1.000	0.000
Day 7	0 (0-0)	0 (0-0)	0 (0-0)	0 (0 – 0)	1.000	0.000
1 Month	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	1.000	0.000

*:P ≤ 0.05 significant, Different superscripts in the same row represent a statistically significant difference between values.

ACP - Amorphous calcium phosphate

Figure 3. Box plot representing pain scores in different groups in the form of median and IQR values before dental bleaching, immediately, day and 2 days after bleaching (Stars represent outliers).

observed in the pain scores after bleaching from day 2 to days 3, 4, 5, 6, 7 and 1 month.

Similarly, there was no statistically significant variation in pain score in the **ACP gel before and after bleaching** group

after bleaching over time (P-value of < 0.001, Effect size of 0.484). A comparison of the time points shows that the mean pain scores instantly after bleaching increased statistically significantly followed by a statistically significant reduction in pain results after the first day. Days 1 to 2 did not alter the

Table 4. Median, Inter-Quartile Range (IQR) and results of Friedman's test for comparison between sensitivity scores at different follow up periods within each group.

Time	ACP gel before bleaching (n = 9)	ACP gel before & after bleaching (n = 9)	ACP gel after bleaching (n = 9)	Glycerin before & after bleaching (n = 9)
Before bleaching	0 (0 – 0) ^B	0 (0 – 0) ^B	0 (0 – 0) ^C	0 (0 – 0) ^C
Immediately Post bleaching	4 (3.5 – 4.5) ^A	3 (0 – 4) ^A	5 (4 – 6.5) ^A	5 (5 – 7) ^A
1 Day	1 (0.5 – 1.5) ^B	0 (0 – 1) ^B	2 (1 – 2.5) ^B	3 (2 – 3.5) ^B
2 Days	0 (0 – 0.5) ^B	0 (0 – 0) ^B	0 (0-0) ^C	0 (0 – 1) ^C
3 Days	0 (0-0) ^B	0 (0-0) ^B	0 (0-0) ^C	0 (0-0) ^C
4 Days	0 (0-0) ^B	0 (0-0) ^B	0 (0-0) ^C	0 (0-0) ^C
5 Days	0 (0-0) ^B	0 (0-0) ^B	0 (0-0) ^C	0 (0-0) ^C
6 Days	0 (0-0) ^B	0 (0-0) ^B	0 (0-0) ^C	0 (0-0) ^C
7 Days	0 (0-0) ^B	0 (0-0) ^B	0 (0-0) ^C	0 (0-0) ^C
1 Month	0 (0-0) ^B	0 (0-0) ^B	0 (0-0) ^C	0 (0-0) ^C
P-value	<0.001*	<0.001*	<0.001*	<0.001*
Effect size (W)	0.437	0.484	0.298	0.466

*: Significant at $P \leq 0.05$, Different superscripts in the same column indicate statistical significant differences between values

ACP - Amorphous calcium phosphate

Figure 4. Line chart representing changes in median sensitivity scores in the four groups at different follow up times.

pain results statistically significantly. No statistically significant changes to pain values after bleaching occurred from day 2 to days 3, 4, 5, 6, 7 and 1 month, as all the cases did not have any pain.

With regard to the **ACP gel after bleaching** group, the median pain scores over time (P -value < 0.001, Effect size= 0.298) changed significantly. The comparison between time intervals indicates that median pain scores were statistically significantly increased instantly after bleaching, and that the pain

scores decreased statistically significantly after 1 day and from 1 to 2 days. Between day 1 and day 2, there was no statistically significant shift in pain rates.

No statistically significant changes in pain scores after bleaching occurred between day 2 and days 3, 4, 5, 6, 7 and 1 month, as there was no pain in all cases.

In the same way, the median pain results changed over time (P -value < 0.001, Effect size = 0.466) in the **glycerin before**

and after bleaching group. A pairwise comparison between times showed that the median pain scores results increased statistically significantly immediately after the bleaching and then decreased after 1 day and from 1 day to 2 days. No significant changes in pain scores were observed from 2 days to 3 days.

Tooth color related data

Change in Classical shade guide Units

Comparison between interventions. Results of changes in tooth shade across groups are presented in Table 5 and Figure 5. There was no statistically significant difference between the

groups immediately post bleaching, after 1 day and 1 week (P-value = 0.828, Effect size = 0.066), 1 month (P-value = 0.426, Effect size = 0.007), or 6 months (P-value = 0.024, Effect size = 0.202). Pair-wise comparison between the groups revealed that the ACP gel before & after bleaching group showed the statistically significantly highest median change in classical shade guide score. ACP gel after bleaching group showed a lower median change in shade, followed by the ACP gel before bleaching group which where statistical significant. Glycerin before & after bleaching group showed the lowest median change in shade guide score.

Table 5. Median, Inter-Quartile Range (IQR) and results of Kruskal-Wallis test for comparison between changes in classical shade guide units in the four groups.

Time	ACP gel before bleaching (n = 9)	ACP gel before & after bleaching (n = 9)	ACP gel after bleaching (n = 9)	Glycerin before & after bleaching (n = 9)	P-value	Effect size (Eta Squared)
Post bleaching	-8 (-11 – -6.5)	-11 (-11.5 – -7.5)	-9 (-12.5 – -6.5)	-10 (-12 – -6.5)	0.828	0.066
1 Day	-8 (-11 – -6.5)	-11 (-11.5 – -7.5)	-9 (-12.5 – -6.5)	-10 (-12 – -6.5)	0.828	0.066
1 Week	-8 (-11 – -6.5)	-11 (-11.5 – -7.5)	-9 (-12.5 – -6.5)	-10 (-12 – -6.5)	0.828	0.066
1 Month	-8 (-10.5 – -6)	-11 (-11.5 – -7.5)	-9 (-11.5 – -6.5)	-7 (-11 – -6)	0.426	0.007
6 Months	-7 (-10.5 – -5) C	-11 (-12.5 – -7) A	-8 (-10 – -6) B	-4 (-7.5 – -1.5) D	0.024*	0.202

*: Significant at $P \leq 0.05$, Different superscripts in the same row are statistically significantly different

ACP - Amorphous calcium phosphate

Figure 5. Box plot representing median and IQR values for changes in classic shade guide units in the different groups (Circles represent outliers).

Discussion

The in-office bleaching method offers great efficiency, using hydrogen peroxide with elevated concentrations of 25 to 40%³. High-concentration bleaching agents, however, cause tooth sensitivity, which is the primary adverse impact associated with in-office bleaching, during and up to 24 hours following the bleaching operation. This sensitivity is associated with the pulp tissue inflammation phase^{11,12}.

In each clinical session, 30% hydrogen peroxide in-office bleaching was performed according to the guidelines of the manufacturer for three 15-minute sessions in this research. Several studies have implemented hydrogen peroxide in three 15-minute sessions^{13–16}. H₂O₂ produces free radicals, which interact with pigment molecules to have a whitening impact. These free radicals in the bleaching gel break down the double bonds between pigment molecules and change the arrangement and/or size of the pigment molecules, creating a more white tooth appearance¹⁷.

The release of cell-derived factors, such as ATP and prostaglandins, can be caused by tooth bleaching. This interaction can cause pulp nociceptors to be excited or sensitized, and harm the pulp tissue¹⁸. Another hypothesis is presently not well recognized; i.e., that the hydrodynamics activate the intradental nerve and release neuropeptide in reaction to this operation³.

Potassium nitrate and sodium fluoride are often used to treat tooth sensitivity as desensitizing agents. These agents can be contained in a bleaching gel and supplied during therapy with a custom tray, or applied separately by being placed in the mouth of the subject for a brief period of time prior to bleaching^{19,20}. In contrast, fluoride used as a desensitizing agents treats tooth sensitivity by blocking exposed dentinal tubules or decreasing liquid pulp flow and blocking stimulus transmission⁶.

The mechanism by which potassium nitrate operates is still not known. Various randomized clinical studies to assess the effectiveness of tooth bleaching have been released, reporting that the use of potassium nitrate and sodium fluoride eliminate post bleaching hypersensitivity^{14,16,18,20–23}. A systemic review and meta-analysis assessed the effectiveness of potassium nitrate and sodium fluoride as desensitizing agents in tooth bleaching therapy and concluded that potassium nitrate and +/-sodium fluoride decrease tooth sensitivity²⁴.

The supply of Ca and PO₄ ions, by means of ACP technology, together with whitening processes can be useful to minimize the loss of minerals as well as the occurrence of roughness and erosion in the dental structure due to whitening²⁵. There is limited research on the application of ACP, bioactive materials, CCP-ACP, bio-glass and bio-glass ceramics as desensitizing agents and re-mineralizing agents⁷.

The primary aim of these products is to encourage dental structural remineralization through the creation of an amorphous

calcium phosphate layer on the surface of the product, initiating apathetic crystallization. This method of remineralization seems far more efficient than sodium nitrate or fluoride alone²⁶, as it not only helps to alleviate the pain, but also stops it from beginning. (Zhao *et al.* 2011)²⁷ They reviewed the application of amorphous calcium phosphate in dentistry and found that, as a result of increasing microcrystalline, ACP is converted readily into a crystalline phase, such as octacalcium phosphate and apatite.

A study by Kwon *et al.*, 2016²⁸ evaluated the time taken by potassium nitrate to reach the pulp cavity and the impact of penetration concentrations on tooth whitening. Relief ACP was used for 0, 5, 15, 30 and 60 minutes before bleaching. The study concluded that, as early as 5 minutes after application, potassium nitrate penetrates into the pulp cavity, and potassium nitrate pretreatment with desensitizers had no adverse effect on the efficacy of tooth whitening. Similar penetration times for hydrogen peroxide and the penetration of potassium nitrate can be described by the small molecular weights of both 34.40 grams per mol and 101.10 grams per mol, respectively; and also, as water soluble agents, their transport into the tooth can be facilitated²⁸. The present clinical trial used oral Relief ACP® gel as a desensitizing agent that, according to the manufacturer, includes 5% potassium nitrate, 0.22% sodium fluoride and 0.75% amorphous calcium phosphate (ACP)⁴.

In the present trial, a VAS scale was used, as a great deal of proof is available to support the pain intensity validity of VAS. Such scales show benefits over other pain intensity self-reporting measures and pain-controlled behavior^{29,30}. Many studies have used the VAS scale to assess dental sensitivity intensity after office bleaching^{8,9,14,31–34}. Others have used both the visual analog scale (VAS) and numerical scale (NRS)^{16,23}.

In this study, participant ages in all groups ranged from 18–40 years old. The mean of ages of patients were 32.4± 4.3, 32.1 ± 4.4, 33.1 ± 4.8 and 32.1± 5.3 for the ACP gel before bleaching group, ACP gel before and after bleaching group, ACP gel after bleaching group and control group, respectively, with no statistically significant difference regarding mean age values (*P*-value = 0.965) between all groups. A recent review was conducted in 35 (Rezende *et al.*, 2016). Regarding the participants' ages, the authors did not find any link between age and the risk or level of tooth sensitivity. Regarding gender, 36 patients (30 women and six men) took part in this research. There was no statistical significance in gender distribution among all groups.

However, with the incidence of female patients in this research distinct outcomes for other population profiles can be noted. Furthermore, socio-cultural beliefs about femininity and men also seem to be an important factor in pain response between the sexes, as the social acceptance of pain expression among females is usually more acceptable—an influence that could lead to biased pain reporting³⁶. The highest average pain score was found in the ACP gel after bleaching and Glycerin before and after bleaching groups, showing the highest median pain

score. The lowest average pain score was shown in the ACP gel applied before and after bleaching group. As mentioned above, potassium nitrate has advantages as a product in that it reduces tooth sensitivity after dental bleaching; several clinical studies have reported this^{14,16,18,20–23}. Moreover, the efficacy of potassium nitrate and sodium fluoride as desensitizing agents was measured in a systematic review meta-analysis²⁴. These studies cannot be directly compared with this clinical trial, as the Relief ACP[®] oral care used as a desensitizing agent includes in its ingredients 5% potassium nitrate, 0.22% sodium fluoride and 0.75% amorphous calcium phosphate (ACP).

In this research, hypersensitivity for all participants tested was not reported by the end of the seven days of the trial. This conclusion was consistent with that in Martin *et al.*, and Farag *et al.*^{8,37}.

In a control group in which glycerin was used as a placebo before and after in-office bleaching, a hypersensitivity enhancement was noted. This may be the result of the placebo or Hawthorne effect. The Hawthorne effect can be defined as an unconscious shift in the participant because of the simple understanding of being observed during a clinical trial³⁸.

Strength and limitations

This trial was a randomized clinical trial with a comparatively large sample of patients, performed in a clinical setting. This was the first clinical study to use a desensitizing agent before and after in-office bleaching to reduce hypersensitivity after bleaching. The median age for patients in this study was 32, and this affects the generalizability of the results to the general population and can be regarded as a study limitation. The following limitation should be considered: the generalizability of results may be limited given the number of female participants was much higher than male participants. We assessed one bleaching product, Dash[™] whitening gel; different bleaching gels and concentrations are likely to affect sensitivity. A randomized clinical trial should therefore be performed with various bleaching products and demographic profiles using other equivalent measures.

Conclusion

The application of the desensitizing agent before and after bleaching was found within the limitations of this research, to be effective in reducing post-bleaching hypersensitivity. Hypersensitivity in all groups gradually decrease two days after in-office bleaching.

Consent

Written approval was acquired from patients to publish their clinical information and clinical images.

Data availability

Underlying data

Open Science Framework: Evaluation of post-bleaching hypersensitivity using desensitizing agent before and /or after in-office bleaching: A randomized clinical trial. <https://doi.org/10.17605/OSF.IO/XUB25>¹⁰

The project contains the following underlying data:

- Results data
 - Results raw.xlsx (Spreadsheet of tooth Sensitivity scores using VAS scale)
 - Age and gender.xlsx (Spreadsheet of age and gender data for study participants)
 - Color measurments.xlsx (Spreadsheet of color changes for study participants)

Extended data

Open Science Framework: Evaluation of post-bleaching hypersensitivity using desensitizing agent before and /or after in-office bleaching: A randomized clinical trial. <https://doi.org/10.17605/OSF.IO/XUB25>¹⁰

This project contains the following extended data:

- Supplementary files
 - Assessor chart (Word document containing chart used by assessor to record patient data)
 - Pain diary (Word document containing pain diary with VAS scales used by participants)
 - Medical and dental health charts (Word document containing chart used to record medical and dental data for participants on requirement)

Reporting guidelines

Open Science Framework: CONCORD checklist and flow diagram for Evaluation of post-bleaching hypersensitivity using desensitizing agent before and /or after in-office bleaching: A randomized clinical trial. <https://doi.org/10.17605/OSF.IO/XUB25>¹⁰

Data are available under the terms of the [Creative Commons Zero “No rights reserved” data waiver](#) (CC0 1.0 Public domain dedication).

References

1. Yan M, Yu Y, Zhang G, *et al.*: **A journey from dental pulp stem cells to a bio-tooth.** *Stem Cell Rev Rep.* 2011; 7(1): 161–71. [PubMed Abstract](#) | [Publisher Full Text](#)
2. Brännström M: **The hydrodynamic theory of dentinal pain: sensation in preparations, caries, and the dentinal crack syndrome.** *J Endod.* 1986; 12(10): 453–7. Brännström, M. (1986). [PubMed Abstract](#) | [Publisher Full Text](#)
3. Markowitz K: **Pretty painful: why does tooth bleaching hurt?** *Med Hypotheses.* 2010; 74(5): 835–40. [PubMed Abstract](#) | [Publisher Full Text](#)

4. Pinheiro HB, Lopes B, Klautau EB, *et al.*: **Influence of bioactive materials used on the dentin surface whitened with carbamide peroxide 16%.** *Mater Res.* 2010; **13**(2): 273–278.
[PubMed Abstract](#) | [Publisher Full Text](#)
5. Haywood VB, Caughman WF, Frazier KB, *et al.*: **Tray delivery of potassium nitrate-fluoride to reduce bleaching sensitivity.** *Quintessence Int.* 2001; **32**(2): 105–9.
[PubMed Abstract](#)
6. Saylor CD, Overman PR: **Dentinal Hypersensitivity: A Review.** *RDH.* 2011; **31**(3): 1–11.
[Reference Source](#)
7. Rahiotis C, Vougiouklakis G: **Effect of a CPP-ACP agent on the demineralization and remineralization of dentine in vitro.** *J Dent.* 2007; **35**(8): 695–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
8. Martin J, Fernandez E, Bahamondes V, *et al.*: **Dentin hypersensitivity after teeth bleaching with in-office systems.** Randomized clinical trial. *Am J Dent.* 2013; **26**(1): 10–4.
[PubMed Abstract](#)
9. Pintado-Palomino K, P Filho O, Zanotto ED, *et al.*: **A clinical, randomized, controlled study on the use of desensitizing agents during tooth bleaching.** *J Dent.* 2015; **43**(9): 1099–1105.
[PubMed Abstract](#) | [Publisher Full Text](#)
10. Tadtos S: **Evaluation of post-bleaching hypersensitivity using desensitizing agent before and / or after in-office bleaching: A randomized clinical trial.** 2019. <http://www.doi.org/10.17605/OSF.IO/XUB25>
11. Loguercio AD, Martins LM, Silva LM, *et al.*: **In-Office Whitening.** *Tooth Whitening.* 2016; 145–167.
[Publisher Full Text](#)
12. Blind S, Trial RC, Calixto AL, *et al.*: **Comparison of the Effects of In-office Bleaching Times on Whitening and Tooth Sensitivity: A Comparison of the Effects of In- office Bleaching Times on Whitening and Tooth Sensitivity: A Single Blind , Randomized Clinical.** *Oper Dent.* 2016; **41**(2): 138–145.
[Publisher Full Text](#)
13. Marson FC, Sensi LG, Vieira LCC, *et al.*: **Clinical evaluation of in-office dental bleaching treatments with and without the use of light-activation sources.** *Oper Dent.* 2008; **33**(1): 15–22.
[PubMed Abstract](#) | [Publisher Full Text](#)
14. Tay LY, Kose C, Loguercio AD, *et al.*: **Assessing the effect of a desensitizing agent used before in-office tooth bleaching.** *J Am Dent Assoc.* 2009; **140**(10): 1245–51.
[PubMed Abstract](#) | [Publisher Full Text](#)
15. Ontiveros JC: **In-office vital bleaching with adjunct light.** *Dent Clin North Am.* 2011; **55**(2): 241–53.
[PubMed Abstract](#) | [Publisher Full Text](#)
16. Parreiras SO, Szesz AL, Farago PV, *et al.*: **Effect of an experimental desensitizing agent on reduction of bleaching-induced tooth sensitivity: A triple-blind randomized clinical trial.** *J Am Dent Assoc.* 2018; **149**(4): 281–290.
[PubMed Abstract](#) | [Publisher Full Text](#)
17. Li Y, Greenwall L: **Safety issues of tooth whitening using peroxide-based materials.** *Br Dent J.* 2013; **215**(1): 29–34.
[PubMed Abstract](#) | [Publisher Full Text](#)
18. Reis A, Dalanhol AP, Kossatz S, *et al.*: **Assessment of tooth sensitivity using a desensitizer before light-activated bleaching.** *Oper Dent.* 2011; **36**(1): 12–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
19. Bonafé E, Loguercio AD, Reis A, *et al.*: **Effectiveness of a desensitizing agent before in-office tooth bleaching in restored teeth.** *Clin Oral Investig.* 2014; **18**(3): 839–45.
[PubMed Abstract](#) | [Publisher Full Text](#)
20. Palé M, Mayoral JR, Llopis J, *et al.*: **Evaluation of the effectiveness of an in-office bleaching system and the effect of potassium nitrate as a desensitizing agent.** *Odontology.* 2014; **102**(2): 203–10.
[PubMed Abstract](#) | [Publisher Full Text](#)
21. Mondelli RF, Azevedo JF, Francisconi AC: **Comparative clinical study of the effectiveness of different dental bleaching methods - two year follow-up.** *J Appl Oral Sci.* 2012; **20**(4): 435–43.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
22. Brignardello-Petersen R: **Desensitizing gel reduces the risk of experiencing dentin hypersensitivity and results in a small decrease in hypersensitivity levels after tooth bleaching.** *J Am Dent Assoc.* 2018; **149**(10): e136.
[PubMed Abstract](#) | [Publisher Full Text](#)
23. da Costa Poubel LA, de Gouvea CVD, Calazans FS, *et al.*: **Pre-operative use of dexamethasone does not reduce incidence or intensity of bleaching-induced tooth sensitivity. A triple-blind, parallel-design, randomized clinical trial.** *Clin Oral Investig.* 2019; **23**(1): 435–444.
[PubMed Abstract](#) | [Publisher Full Text](#)
24. Wang Y, Gao J, Jiang T, *et al.*: **Evaluation of the efficacy of potassium nitrate and sodium fluoride as desensitizing agents during tooth bleaching treatment — A systematic review and meta-analysis.** *J Dent.* 2015; **43**(8): 913–23.
[PubMed Abstract](#) | [Publisher Full Text](#)
25. Giniger M, Macdonald J, Ziemba S, *et al.*: **The clinical performance of professionally dispensed bleaching gel with added amorphous calcium phosphate.** *J Am Dent Assoc.* 2005; **136**(3): 383–92.
[PubMed Abstract](#) | [Publisher Full Text](#)
26. Tschoppe P, Neumann K, Mueller J, *et al.*: **Effect of fluoridated bleaching gels on the remineralization of predemineralized bovine enamel in vitro.** *J Dent.* 2009; **37**(2): 156–62.
[PubMed Abstract](#) | [Publisher Full Text](#)
27. Zhao J, Liu Y, Sun WB, *et al.*: **Amorphous calcium phosphate and its application in dentistry.** *Chem Cent J.* 2011; **5**: 40.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
28. Kwon SR, Dawson DV, Wertz PW: **Time Course of Potassium Nitrate Penetration into the Pulp Cavity and the Effect of Penetration Levels on Tooth Whitening Efficacy.** *J Esthet Restor Dent.* 2016; **28** Suppl 1: S14–22.
[PubMed Abstract](#) | [Publisher Full Text](#)
29. Jensen MP, Karoly P, Braver S: **The measurement of clinical pain intensity: a comparison of six methods.** *Pain.* 1986; **27**(1): 117–126.
[PubMed Abstract](#) | [Publisher Full Text](#)
30. Hjermstad MJ, Fayers PM, Haugen DF, *et al.*: **Studies comparing Numerical Rating Scales, Verbal Rating Scales, and Visual Analogue Scales for assessment of pain intensity in adults: a systematic literature review.** *J Pain Symptom Manage.* 2011; **41**(6): 1073–1093.
[PubMed Abstract](#) | [Publisher Full Text](#)
31. Thiesen CH, Rodrigues Filho R, Prates LH, *et al.*: **The influence of desensitizing dentifrices on pain induced by in-office bleaching.** *Braz Oral Res.* 2013; **27**(6): 517–523.
[PubMed Abstract](#) | [Publisher Full Text](#)
32. Maghbrah GA, Alzraikat H, Guidoum A: **Assessment of the effect of casein phosphopeptide-amorphous calcium phosphate on postoperative sensitivity associated with in-office vital tooth whitening.** *Oper Dent.* 2014; **39**(3): 239–47.
[PubMed Abstract](#) | [Publisher Full Text](#)
33. Hegde V, Murkey L: **Evaluation of residual root canal filling material after retreatment of canals filled with hydrophilic and hydrophobic obturating system: An in vitro scanning electron microscopy study.** *Endodontology.* 2017; **29**(1): 47.
[Reference Source](#)
34. Lima SNL, Ribeiro IS, Grisotto MA, *et al.*: **Evaluation of several clinical parameters after bleaching with hydrogen peroxide at different concentrations: A randomized clinical trial.** *J Dent.* 2018; **68**: 91–97.
[PubMed Abstract](#) | [Publisher Full Text](#)
35. Rezende M, Loguercio AD, Kossatz S, *et al.*: **Predictive factors on the efficacy and risk/intensity of tooth sensitivity of dental bleaching: A multi regression and logistic analysis.** *J Dent.* 2016; **45**: 1–6.
[PubMed Abstract](#) | [Publisher Full Text](#)
36. Bartley EJ, Fillingim RB: **Sex differences in pain: a brief review of clinical and experimental findings.** *Br J Anaesth.* 2013; **111**(1): 52–58.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
37. Farag I, Abouelfotouh I, Mohamed O, *et al.*: **A comparative study of different bleaching techniques, regarding the color change, stability and postoperative hypersensitivity: a randomized controlled clinical trial.** *Stomatological Dis Sci.* 2018; **2**: 5.
[Publisher Full Text](#)
38. Talioti E, Hill R, Gillam DG, *et al.*: **The Efficacy of Selected Desensitizing OTC Products: A Systematic Review.** *ISRN Dent.* 2014; **2014**: 865761.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)

Open Peer Review

Current Peer Review Status:

Version 1

Reviewer Report 07 July 2020

<https://doi.org/10.5256/f1000research.22921.r66353>

© 2020 Fernández E. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Eduardo Fernández

Department of Restorative Dentistry, Faculty of Dentistry, University of Chile, Santiago, Chile

- I consider a correct study, justification of the proposal and research question.
- The scales used are adequate and the results expected.
- I am concerned about the low sample size and the statistical power of the conclusions. I think you should add this to the limitations of the study.
- Adequate references, nice work!

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Restorative Dentistry

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 07 Jul 2020

Silvia Sabry Tawfik, Fayoum University, Fayoum, Egypt

Thanks a lot dear professor. Regarding the sample size calculation, it was done by the biostatistics department at the faculty of dentistry, Cairo University. Based on the primary outcome post-bleaching hypersensitivity, based on previous studies^{8,9}.

- Pintado-Palomino, K., Peitl Filho, O., Zanotto, E. D., & Tirapelli, C. (2015). A clinical, randomized, controlled study on the use of desensitizing agents during tooth bleaching. *Journal of dentistry*, 43(9), 1099-1105.
- Martin, J., Fernandez, E., Bahamondes, V., Werner, A., Elphick, K., Oliveira Jr, O. B., & Moncada, G. (2013). Dentin hypersensitivity after teeth bleaching with in-office systems. *Randomized clinical trial. Am J Dent*, 26(1), 10-4.

Competing Interests: No competing interests were disclosed.

Reviewer Report 02 July 2020

<https://doi.org/10.5256/f1000research.22921.r64696>

© 2020 Bersezio C. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Cristian Bersezio

Department of Restorative Dentistry, Faculty of Dentistry, University of Chile, Santiago, Santiago, Chile

Firstly, I congratulate the team of researchers, since all clinical studies present a certain degree of difficulty. There is very interesting data in your research, which I think can be much better used.

1) I suggest that it be reviewed by experts in the translation of scientific manuscripts since there are certain phrases or very colloquial words.

2) In the summary:

- I would delete the word "unfortunately", simply mention that its main adverse effect is tooth sensitivity.

- "N" (uppercase) is used when speaking to the total study population, when determining the number of a group, "n" (lowercase) is used.
- The results should include the most important data and show their numerical values, not just words.

3) In the introduction:

- The definition of dental sensitivity is missing, it talks about the cause but not what it is.
- The objective of the study is clear, I would recommend strengthening the introduction with antecedents on ACP, and formulating a hypothesis based on them.

4) In the methodology: The methodology is very well detailed.

- In the part of the second visit, do not use the term sessions, use the term applications. There are three applications of 15 minutes each, in a single session.
- I recommend using better photographs, they are not very aesthetic. It would have been good without the cotton, the bite rest on the molars performs that function.
- The sample size per group seems to be a little low, I recommend justifying it with other publications.
- The history of dental sensitivity was an Exclusion criterion?
- For the evaluation of the color, the ideal would have been to use the Vita Bleachguide 3D Master guides, it is more precise, and the change value between one unit and the other is the same. On the other hand, as the order by value of the vita classical is suggested, the change in color between one tablet (unit) and another is not the same among all.

5) In the results:

- The results must be summarized, there is an excess of tables and graphs that express practically the same thing. You should choose to use tables or graphs to express the same results. In the written part, the most important thing should be highlighted, not to report all the results that can be seen when reading the tables or graphs.
- Demographic data is best used as a table to express it and should include baseline sensitivity and color data, and analyze whether the groups are the same.
- To express the color change, I recommend using the Δ SGU (difference from the scale guide unit), please review the papers:
Oper Dent. 2019 Nov / Dec; 44 (6): 581-588.¹
Oper Dent. Jan / Feb 2017; 42 (1): 41-52.²

6) In discussion:

- The first part (second to fifth paragraph) are more a theoretical framework than a discussion. It is more appropriate to use it in the introduction to justify a hypothesis or the use of that desensitizer. It should be summarized and used in the introduction.

- Theoretical content can be used to justify the results, but it must be related. For this, the first part of the discussion always remembers the research question and then answers it, and based on that the results can be explained.
- Although effectiveness is a secondary result, this must be discussed. Especially since the placebo group has a greater recurrence of color over time. It is interesting to analyze and provides valuable information.

Major changes are required in the preparation of the manuscript for publication, which can be modified by the authors.

References

1. Bersezio C, Estay J, Sáez M, Sánchez F, et al.: Six-month Follow-up of the Effect of Nonvital Bleaching on IL-1 β and RANK-L: A Randomized Clinical Trial. *Oper Dent*. **44** (6): 581-588 [PubMed Abstract](#) | [Publisher Full Text](#)
2. Fernández E, Bersezio C, Bottner J, Avalos F, et al.: Longevity, Esthetic Perception, and Psychosocial Impact of Teeth Bleaching by Low (6%) Hydrogen Peroxide Concentration for In-office Treatment: A Randomized Clinical Trial. *Oper Dent*. **42** (1): 41-52 [PubMed Abstract](#) | [Publisher Full Text](#)

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Clinical studies, Dental materials, Tooth whitening

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 07 Jul 2020

Silvia Sabry Tawfik, Fayoum University, Fayoum, Egypt

Thanks a lot, dear professor for your meticulous & great review. I'll do my best to rephrase & correct all the points you have mentioned.

Competing Interests: No competing interests were disclosed.

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com

F1000Research