Bleaching in vital teeth: a systematic review

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There are mainly three approaches by which teeth whitening treatments can be carried out: in-office, at-home and via over-the-counter (OTC) products. There are conflicting opinions in the literature on which treatments are most effective and stable over time, and on which ones give greater dental sensitivity during the whitening treatment, this being the main adverse effect of the treatment. The objective of this review was to evaluate the efficacy of post-treatment whitening (primary outcome), its stability after several weeks (secondary outcome) and the prevalence of dental sensitivity (tertiary outcome) in patients undergoing whitening treatment, in order to evaluate which is the most effective and safest whitening approach for patients. The following systematic review was conducted on the basis of the indications of the Prisma protocol; 10 studies were identified through literature searches on the PubMed database. The various procedures related to the studies included in this review have shown that they can produce satisfactory post-treatment whitening efficacy and, albeit with less data available, also in the long term; furthermore, dental sensitivity is present in the first days of application, and tends to disappear after a few days, and its intensity is generally mild to moderate for all the whitening techniques tested. For a better evaluation of the stability over time with the different techniques, it could also be useful to check the eating habits of the patients since the diet could be an important factor that influences the extrinsic staining of the teeth; it is necessary to undertake further research into desensitizing protocols that can further improve patient comfort.

Teeth whitening is one of the aesthetic requests made by patients due to the discoloration process that teeth can undergo. The term “dental discoloration” is used to describe any change in the color or translucency of a tooth, and is generally classified as extrinsic and intrinsic (1).

The extrinsic stains are mainly localized in the film and can be generated by the reaction between sugars and amino acids or acquired by the retention of exogenous chromophores in the film(2); are mainly associated with environmental factors or individual behaviors, such as tobacco use, exposure to metal salts, or consumption of pigmented foods or beverages (3-5).

Intrinsic stains, on the other hand, are integrated into the tooth structure (6); may arise due to systemic conditions, such as genetic diseases affecting the hard tissues of the tooth (e.g., dentinogenesis imperfecta, amelogenesis imperfecta) or local pre-eruptive or post-eruptive factors, such as age or use of tetracyclines in childhood (1,7-9).

Keywords: Vital tooth bleaching; bleaching agents; home bleaching; office bleaching
Vital teeth were whitened as early as the late 1800s using various oxidizing agents, such as oxalic acid; later hydrogen peroxide was used for whitening in the office with a heating tool or with a light source (5). This technique remained the predominant method for teeth whitening until the introduction of an at home approach called “nightguard vital bleaching” in 1989, which used a vacuum-packed plastic tray containing a carbamide peroxide whitening agent (10).

10% carbamide peroxide was first used in the late 1960s when an orthodontist, in-structing his patients to use an “over-the-counter” oral antiseptic containing this molecule for the treatment of gingivitis, found that it not only improved gum health, but also that teeth were whitened (11).

Later an over-the-counter whitening strip was introduced for applying a whitening agent to hydrogen peroxide or low-dose carbamide peroxide (12); this system has become very popular and has been shown to be safe and effective in clinical studies (13). Over-the-counter products also developed whitening toothpastes, which rely mainly on abrasives for mechanical removal of extrinsic surface stains, although some contain low levels of peroxide (14,15). Finally, Power Bleaching is another in-office whitening procedure that uses concentrated solutions of hydrogen peroxide, with or without light activation (16). In-office teeth whitening remains a popular aesthetic procedure and much re-quested by patients because it produces more immediate results, in fewer sessions, than at-home treatment (17), although several clinical studies have demonstrated the efficacy of whitening with both procedures (18-20); even the use of over-the-counter (OTC) products, such as whitening strips, has been shown to have good efficacy (21). Tooth sensitivity is a very common side effect of whitening treatment (22). There are conflicting opinions in the literature on which treatments are most effective and stable over time, and on which ones give greater dental sensitivity during whitening treatment (23).

The objective of this review is to evaluate the effectiveness of post-treatment whitening and its stability after a few weeks in the works that measured the color difference from the baseline with an objective method (spectrophotometer) and expressed as ΔE, and to evaluate the prevalence of dental sensitivity in patients undergoing whitening treatment, in order to evaluate which is the most effective and safest whitening approach for patients.

MATERIALS AND METHODS

The following systematic review was conducted based on the indications of the Prisma protocol. The study was built on the PICO questions of population, intervention, control and outcome: population (adult patients who have undergone vital teeth whitening), inter-vention (Vital tooth bleaching), comparison (different whitening protocols) and outcome (efficacy post-treatment whitening and color stability evaluated by spectrophotometer (ΔE), and prevalence of dental sensitivity).

The formulation of the PICO question is as follows: what is the whitening effec-tiveness of the various vital tooth bleaching protocols (primary outcome)? Other ques-tions were also raised: how stable is the tooth whitening result a few weeks after treatment (secondary outcome) and what is the prevalence of tooth sensitivity in patients (tertiary outcome)? After an initial selection phase of the records identified in the PubMed database, the potential eligible articles are qualitatively evaluated in order to identify the evi-dence-based differences in terms of dental sensitivity and efficacy between the different whitening protocols.

Eligibility criteria

The papers taken into consideration are clinical studies with parallel, split-mouth and opposing-arch design concerning vital tooth bleaching protocols and published with abstracts in English. The potentially eligible articles were finally subjected to a full-text analysis to verify their use for a qualitative and quantitative analysis. The following criteria were applied in the full-text analysis:

- Inclusion: all those studies that evaluated the various vital tooth bleaching protocols in the adult population, whose color change, expressed as ΔE, was objectively evaluated using a spectrophotometer.
- Exclusion: studies on age groups <18 years, in vitro studies, animal studies, studies on patients with severe dental discoulouration (tetracyclines, fluorosis, ...), studies on devitalized or filled teeth, studies written in a language other than ‘English.'
Search strategy

The studies were identified through literature searches on the PubMed database. The search was conducted between 15.12.2021 and 10.01.2022 and the last search for a partial update of the literature was carried out on 14/12/2022. The following search terms were used: “Vital tooth bleaching” (454 records), “External bleaching” (322 records), “tooth discoloration” AND “bleaching agents” (500 records); as a complement to this search, a manual search of the articles included in the bibliographic references of other sources was performed, selecting the citations considered relevant (6 articles), for a total of 1282 articles (Fig. 1).

Screening methodology

Initially, the articles were selected by analyzing the title and abstract according to the research described above and, in doubtful cases, the text was also analyzed to eliminate records not related to the topics of the review. The articles obtained were subject to full-text analysis (67 articles), considered eligible for qualitative analysis for the following three outcomes:

1. Primary outcome, whitening efficacy of the various vital tooth bleaching protocols;
2. Secondary outcome, stability of dental whitening a few weeks after treatment;

RESULTS

After screening the database and manually searching for articles included in references from other sources, 1282 studies were identified (Fig. 2). After the evaluation of the articles by title and abstract, 67 were selected for the evaluation of the full-text, and of these only 10 were selected for qualitative and quantitative analysis.

Characteristics of the included studies

The characteristics of the 10 selected studies are listed in Table 1. The data was collected by first author, date, journal, study design, application...
Table I. Main features of the included studies

<table>
<thead>
<tr>
<th>First Author, Date, Journal</th>
<th>Study design</th>
<th>Application Type</th>
<th>No. of subjects (male/female)</th>
<th>Mean subjects' age ±SD (range) years</th>
<th>Groups/materials</th>
<th>Bleaching protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abouelfotouh IFI, 2018, Stomatological Disease and Science</td>
<td>Parallel</td>
<td>AH; IO; combined</td>
<td>21 (n.r.)</td>
<td>n.r. (18-45)</td>
<td>25% HP with LED irradiation (IO) 9.5% (AH) Combined</td>
<td>IO: 3 x 15-minutes sessions with LED; AH: 30 minutes, twice a day, for 14 day; Combined: 2 x 15-minutes sessions + 30 minutes, twice a day, for another 14 days</td>
</tr>
<tr>
<td>V Alonso de la Peña, 2014, Operative Dentistry</td>
<td>Parallel</td>
<td>AH</td>
<td>96 (28/68)</td>
<td>25.9 ±5.6 (n.r.)</td>
<td>10% CP 15% CP 7.5% HP 9.5% HP</td>
<td>1 h/day, for 2 weeks</td>
</tr>
<tr>
<td>Bernardon JK, 2010, Operative Dentistry</td>
<td>Split-mouth</td>
<td>AH; IO; combined</td>
<td>90 (n.r.)</td>
<td>n.r. (n.r.)</td>
<td>HB/OBL OB/OBL HB/HB+OBL</td>
<td>HB: 8 h/day for 2 weeks OB/OBL: 2 appointment (15-day interval), 3 x 15-minutes applications for each session, without/with light</td>
</tr>
<tr>
<td>Khemiss M, 2021, International Journal of Dentistry</td>
<td>Parallel</td>
<td>OTC</td>
<td>38 (12/26)</td>
<td>26.2 ±4.2 (18-35)</td>
<td>3% CP activated by 5% Lactoperoxidase; Control (sodium fluoride)</td>
<td>Brushing the teeth with the toothpastes 3 times daily, for 3 minutes for 3 weeks</td>
</tr>
<tr>
<td>Meireles SS, 2008, Operative Dentistry; Journal of Dentistry</td>
<td>Parallel</td>
<td>AH</td>
<td>92 (31/61)</td>
<td>25.3 ±7.9 (18-55)</td>
<td>10 % CP 16% CP</td>
<td>2 h/day for 3 weeks</td>
</tr>
<tr>
<td>Moghadam FV, 2013, European Journal of Dentistry</td>
<td>Split-mouth</td>
<td>AH; IO</td>
<td>20 (8/12)</td>
<td>n.r. (18-55)</td>
<td>AH:15% CP IO: 38% HP with LED</td>
<td>AH: 4 h/day for 2 weeks; IO: 3 x 15-min applications and activated by LED curing system</td>
</tr>
<tr>
<td>Ontiveros JC, 2009, Journal of Dentistry</td>
<td>Opposing-arch</td>
<td>IO</td>
<td>20 (n.r.)</td>
<td>n.r. (n.r.)</td>
<td>25% HP with and without light</td>
<td>2 separate 45-min exposures</td>
</tr>
<tr>
<td>Polydorou O, 2013, Operative Dentistry</td>
<td>Parallel</td>
<td>IO</td>
<td>60 (n.r.)</td>
<td>27.64 ±5 (18-70)</td>
<td>38% HP with halogen 38% with laser unit</td>
<td>4 x 15-minutes single visit treatment (halogen for first 8 minutes for each session; laser for the first 30 seconds for each session)</td>
</tr>
<tr>
<td>Tsujimoto A, 2021, American Journal of Dentistry</td>
<td>Parallel</td>
<td>IO</td>
<td>50 (17/33)</td>
<td>n.r. (n.r.)</td>
<td>35% HP with/without halogen lamp</td>
<td>3x15-minutes sessions (with 3 minutes of irradiating light); 3x20-minutes sessions (without light)</td>
</tr>
<tr>
<td>Zekonis R, 2003, Operative Dentistry</td>
<td>Split-mouth</td>
<td>AH; IO</td>
<td>19 (n.r.)</td>
<td>n.r. (n.r.)</td>
<td>10% CP (AH) 35% HP (IO)</td>
<td>AH: trays for 14 nights; IO: two appointments, each with three 10-minutes applications with 7 days between appointment</td>
</tr>
</tbody>
</table>

AH: At-home; IO: In-office; CP: carbamide peroxide; HP: hydrogen peroxide; HB: at-home with 10% CP; OBL: in-office with 35% HP: with light; OB: IO without light; OTC: over the counter. 

Fig. 2. Formation of final products starting from Carbamide peroxide
type, number of subjects (male/female), mean subjects’ age ±SD (range) in years, groups / materials and bleaching protocol.

The parallel study design was predominantly used in six studies (19, 20, 41-45), considering the two study of Meireless SS as one; three studies used the split-mouth design (18, 46, 47), and only one study used the opposing-arch design (48). From six studies it was possible to derive the prevalence of cases in which patients reported dental sensitivity (19, 20, 41, 43, 44, 46, 47).

The smallest number of patients included among these studies is 19 (47), while the study that included the largest number of patients is 96 patients (19); most of the subjects are female, and the mean subjects’ age in the various studies is comparable.

Regarding the type of bleaching agent application, at-home application was used in two studies (19, 20, 43), three studies have used the in-office one (44, 45, 48), two studies evaluated both types of at-home and in-office applications (46, 47), and two other studies, in addition to these two types of application, also evaluated the combination of at-home and in-office application (18, 41); the use of over-the-counter (OTC) products as bleaching agents was evaluated in a single article (42). The use of a light source as an activation of in-office whitening was reported in six studies (18, 41, 44-46, 48). The at-home protocol was performed in most studies for 14 days, while in one study it was performed for 3 weeks (20, 43); the tray at home use time reported in these studies is 1 hour per day (19, 41), 2 hours per day (20, 43), 4 hours per day (46), 8 hours per day (18), while the number of hours of use of a study is not specified (47).

The in-office approach was performed in 1 (41, 44-46) or 2 appointments (18, 47, 48) after 7 days (47) or 15 days (18) the one from the other; in the study by Ontiveros JC and Paravina RD (48), the interval between the two appointments is not reported; the exposure time to the whitening agent in the in-

Table II. Bleaching effectiveness post-treatment, color stability, prevalence of tooth sensitivity

<table>
<thead>
<tr>
<th>First Author, Date, Journal</th>
<th>Bleaching effectiveness ΔE (SD) post-treatment</th>
<th>Color stability ΔE (SD)</th>
<th>Prevalence of tooth sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abouelfotouh IFI, 2018, Stomatological Disease and Science</td>
<td>IO: 8.06 (2.76)  AH: 8.13 (1.21)  Combined: 9.59 (3.95)</td>
<td>6 Months</td>
<td>IO: 100%, AH: 57.1%, Combined: 57.1%</td>
</tr>
<tr>
<td>V Alonso de la Peña, 2014, Operative Dentistry</td>
<td>10% CP: 6.6 (3.5)  15% CP: 6.5 (4.0)  7.5% HP: 7.4 (2.6)  9.5% HP: 7.1 (4.0)</td>
<td>n.r.</td>
<td>10% CP: 54.2%, 15% CP: 54.2%, 7.5% HP: 58.3%, 9.5% HP: 58.3%</td>
</tr>
<tr>
<td>Khemiss M, 2021, International Journal of Dentistry</td>
<td>3%CP: 5.34 (2.31)  Control: 4.32 (1.56)</td>
<td>n.r.</td>
<td>n.r.</td>
</tr>
<tr>
<td>Meireles SS, 2008, Operative Dentistry; Journal of Dentistry</td>
<td>10% CP: 4.3 (1.9)  16% CP: 4.6 (2.0)</td>
<td>6 Months</td>
<td>10% CP: 41.3%, 16% CP: 44.4%</td>
</tr>
<tr>
<td>Polydorou O, 2013, Operative Dentistry</td>
<td>38% HP: 4.8 (3.7)  38% HP with halogen: 6.1 (1.9)  38% HP with laser: 2.15 (2.4)</td>
<td>3 Months</td>
<td>38% HP: 7.05 (2.3)  38% HP with halogen: 5.1 (2.1)  38% HP with laser: 6.7 (2.8)</td>
</tr>
<tr>
<td>Tsujimoto A, 2021, American Journal of Dentistry</td>
<td>With light: 3.40 (1.58)  Without light: 3.30 (1.54)</td>
<td>6 Months</td>
<td>With light: 3.09 (1.60)  Without light: 2.91 (1.12)</td>
</tr>
<tr>
<td>Žekonis R, 2003, Operative Dentistry</td>
<td>AH: 12.32 (2.89)  IO: 5.32 (1.93)</td>
<td>12 Weeks</td>
<td>IO: 15.8%, AH: 10.5%</td>
</tr>
</tbody>
</table>
It is believed that the whitening process occurs when the reactive oxygen molecules generated by hydrogen peroxide attack the pigmented organic molecules in the spaces between the inorganic salts in the tooth enamel by attacking the double bonds of the chromophore molecules (17, 29); this involves the splitting of the chromophore molecules into smaller and less pigmented constituents, which will result in a change in the absorption spectrum of the chromophore molecules with consequent whitening of the dental tissues (5).

The release of ammonia and carbon dioxide from urea plays an important role in preserving the structure of the dental tissues as it elevates the pH of the whitening agent in the oral cavity to a more basic environment within 15 minutes (30).

There are mainly three approaches by which teeth whitening treatments can be carried out:

- “in-office” or “dentist-supervised in-office whitening”
- “at-home” or “home treatment supervised by the dentist”
- through over-the-counter (OTC) products, which can be used by patients without any supervision by the dentist (21, 31).

The in-office approach involves the use of highly concentrated hydrogen peroxide (greater than 30%) or highly concentrated carbamide peroxide (greater than 37%) in one or three clinical appointments of 30-50 minutes each, at a distance 2-7 days (5, 32); moreover, the peroxide may or may not be activated by heat or light (33).

The at-home treatment, on the other hand, involves the home use of the whitening gel at lower concentrations (10-20% carbamide peroxide) positioned in custom-made masks, and whose daily application time varies depending on the concentration of the product for at least two weeks; this technique has been used for many decades and is probably the most widespread (34).

Bleaching effectiveness post-treatment, color stability, prevalence of tooth sensitivity

Table 2 shows the data relating to bleaching effectiveness post-treatment, color stability, both expressed as ΔE, and to the prevalence of tooth sensitivity.

In 3 studies, no follow-up was carried out, therefore the data relating to color stability was not reported (37, 42, 48); however, the prevalence of tooth sensitivity data in 4 studies were not reported (36, 42, 45, 48).

DISCUSSION

From the analysis of the literature it emerges that current teeth whitening materials almost exclusively use peroxide compounds as an active ingredient, and in particular carbamide peroxide and hydrogen peroxide are the most commonly used (24).

The whitening action in chemically induced whitening is mainly due to the effects of carbamide peroxide, which releases approximately 33% of its content as hydrogen peroxide (H2O2), which can act as a powerful oxidant and which forms free radicals such as hydroxyl radicals and perhydroxyl and superoxide anions (25), reactive oxygen molecules which are unstable and transformed into oxygen and hydrogen peroxide anions (26). Furthermore, carbamide peroxide also releases urea, which is rapidly decomposed into carbon dioxide and ammonia (17, 27) (Figure 2).

Hydrogen peroxide crosses the enamel-dentinal junction and interacts in the un-derlying dentin with the chromophores, pigments and ions that are recognized to be responsible for tooth staining (28); it is believed that the whitening process occurs when the reactive oxygen molecules generated by hydrogen peroxide attack the pigmented organic molecules in the spaces between the inorganic salts in the tooth enamel by attacking the double bonds of the chromophore molecules (17, 29); this involves the splitting of the chromophore molecules into smaller and less pigmented constituents, which will result in a change in the absorption spectrum of the chromophore molecules with consequent whitening of the dental tissues (5).

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The association between in-office and at-home procedures has also been suggested to speed up the whitening process (35, 36) as more than one session is usually required. office and some time is needed between consecutive sessions for the reduction of pulp inflammation caused by the high concentrations.
of peroxides that delay treatment (37, 38).

Finally, a variety of over-the-counter (OTC) products are available which include strips, paints, mouthwashes, chewing gums, whitening toothpastes, dental floss whiteners (1), which can be easily applied at home by the patient. Whitening toothpaste is the most common over-the-counter product, containing abrasives for stain removal in combination with reduced amounts of whitening agents (39) similarly found in other products (6, 40).

In particular, the analysis of the scientific literature has identified very heterogeneous procedures in the various studies included (which is why summarizing the data in a meta-analysis results in a high risk of bias between the studies), even within the same type of question example, tray at home use reported in these studies is 1 hour per day (37, 41), 2 hours per day (38, 43), 4 hours per day (46), 8 hours per day (36); another example of heterogeneity is due to the time interval between one session and another of in-office treatment, which in one study was 7 days (47) while in another study it was 15 days (36).

The measurement of the color difference following bleaching in the studies of this review was carried out with the CIELAB system (49).

ΔE is the color difference between two objects and can be calculated within the CIELAB system (49). The naked eye is able to distinguish color differences if the ΔE value is greater than 3.3 (50), therefore small color variations could not be perceived; instead, the spectrophotometer is considered the most reliable measurement tool because it is more objective and more precise than observations of the human eye or conventional techniques (51, 52).

The whitening system that uses light (LED, laser, halogen) as a lightening accelerator has been used in most of the studies evaluating in-office treatment (36, 41, 44-46, 48); in the literature it has been stated that the use of a light source accelerates the whitening process (29), although in this study the results obtained are comparable with those without the use of light, as also confirmed from other research projects (53, 54). It has been stated that LED is the most favorable light source as it emits high-energy blue light which stimulates the decomposition of hydrogen peroxide without producing heat (5); in an in vitro study, the use of LED light did not show a significant increase in the intrapulpary temperature of the teeth when used for the recommended exposure time (55).

The higher concentration of hydrogen peroxide used in in-office treatments gives evident results in a shorter exposure time; however, the short exposure time to a high concentration can be compensated for by a lower concentration of the bleaching agent and longer exposure times (56). The effect of the high concentration could be explained by the dehydration of the teeth that these concentrations cause after whitening (57).

Khemiss et al (42) reported that the ΔE of a whitening toothpaste containing 3% CP and 5% lactoperoxidase was higher than a non-whitening toothpaste, although an improvement in tooth color was also recorded with this type of toothpaste, attributable both to the cleansing properties of normal toothpaste and to the optimal oral hygiene of patients (58, 59). Whitening toothpastes generally rely on abrasives for mechanical removal of extrinsic stains, but low levels of peroxide may also be present to help lighten tooth color (15, 34); activating agents, such as chemicals and enzymes, can also be added, which can activate whitening; lactoperoxidase is one of the enzymes that can be used for this purpose (58, 60).

One of the side effects of vital teeth whitening is tooth sensitivity (26, 61); this finding was also confirmed by the studies considered in this review. Patient-reported sensitivity assessment can be recorded using several methods: ‘‘Yes’’ or ‘‘No, ‘’ (62), scale from 0 (none) to 4 (severe) (38) and scale from 0 to 10 (high hypersensitivity) (63).

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The sensitivity of the teeth may be associated with the heating of the whitening agent due to the use of a light source (53, 61); in the study by Polydorou O et al (44), in which three whitening protocols with 38% HP were compared with halogen, laser and without light, only laser whitening resulted in the sensitivity of the teeth during the procedure; this can be explained by the increase in pulp temperature resulting from the use of the laser, even if it is not the only trigger, as the use of a highly concentrated whitening agent is a factor that favors dental sensitivity (29); in fact it has been shown that peroxide diffuses into enamel and dentin and reaches
the pulp, in an amount and with effects correlated to the concentration of the whitening agent (20); despite this, even the low concentrations used in home treatment caused dental hypersensitivity in the patients in the different studies; in fact, in this case, the low concentration is compensated by the longer exposure time with home treatment which leads to sensitivity levels comparable to those resulting from treatment at higher concentrations (64). To reduce dental sensitivity, many whitening agents have potassium and / or sodium nitrate in their composition, associated with lower risk and intensity of tooth sensitivity in both in-office and at-home whitening (65, 66).

In the studies of this review which reported the prevalence of dental hypersensitivity, this is present in the first days of application, and tends to disappear over time, and its intensity is generally mild to moderate for all the bleaching techniques tested.

All these studies showing that the various techniques can produce a satisfactory post-treatment whitening efficacy and, albeit with less data available, even in the long term, even if diet has not been considered, which could be a determining factor in dis-coloration. dental after treatment (67).

Authors should discuss the results and how they can be interpreted from the per-spective of previous studies and of the working hypotheses. The findings and their im-plications should be discussed in the broadest context possible. Future research direc-tions may also be highlighted.

Within the limitations of the present study, the different bleaching techniques tested showed similar clinical efficiency and color stability over time; furthermore, the various whitening techniques tested showed a similar degree of dental hypersensitivity. For a better evaluation of the stability over time with the different techniques, it could also be useful to check the eating habits of the patients since the diet could be an important factor that influences the extrinsic staining of the teeth. Further research into desensitizing protocols that can further improve patient comfort needs to be addressed.

Conflicts of Interest
The authors declare no conflicts of interest.

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