DR. CARLOS MIGUEL MARTO (Orcid ID : 0000-0001-9269-5417)

Article type : Review

Title: Evaluation of the efficacy of dentin hypersensitivity treatments - a systematic review and follow-up analysis

Short running title: Evaluation of dentin hypersensitivity treatments

AUTHORS: Carlos Miguel Marto[a,b,c,d,§*], Anabela Baptista Paula[a,b,c,§], Tiago Nunes[a], Miguel Pimenta[a], Ana Margarida Abrantes[b,c,e], Ana Salomé Pires[b,c,e], Mafalda Laranjo[b,c,e], Ana Coelho[a,b,c], Helena Donato[f], Maria Filomena Botelho[b,c,e], Manuel Marques Ferreira[b,c,g], Eunice Carrilho[a,b,c]

§ These authors contributed equally for this work

a Institute of Integrated Clinical Practice, Faculty of Medicine, University of Coimbra, Coimbra, Portugal
b Institute for Clinical and Biomedical Research (iCBR), area of Environment, Genetics and Oncobiology (CIMAGO), Faculty of Medicine, University of Coimbra, Coimbra, Portugal
c CNC.IBILI, University of Coimbra, Coimbra, Portugal
d Experimental Pathology Institute, Faculty of Medicine, University of Coimbra, Coimbra, Portugal
e Biophysics Institute, Faculty of Medicine, University of Coimbra, Coimbra, Portugal
f Documentation Department, Coimbra Hospital University Centre, Coimbra, Portugal
g Institute of Endodontics, Faculty of Medicine, University of Coimbra, Coimbra, Portugal

*** Corresponding author:** Carlos Miguel Marto
E-mail adress: cmiguel.marto@uc.pt
Phone: +351-239 857 700 Fax: +351-239 857 745
Instituto de Patologia Experimental,
Faculdade de Medicina da Universidade de Coimbra, Pólo III
Azinhaga de Santa Comba, Celas
3000-548 Coimbra

Carlos Miguel Marto
Institute of Experimental Pathology
Instituto de Patologia Experimental
Faculdade de Medicina da Universidade de Coimbra, Pólo III
Azinhaga de Santa Comba, Celas
3000-548 Coimbra

Anabela Batista Paula; Tiago Nunes; Miguel Pimenta; Ana Coelho; Eunice Carrilho
Institute of Integrated Clinical Practice
Instituto de Clínica Integrada, Área de Medicina Dentária
Av. Bissaya Barreto, Bloco de Celas
3000-075 Coimbra

Ana Margarida Abrantes; Ana Salomé Pires; Mafalda Laranjo; Maria Filomena Botelho
Biophysics Institute
Instituto de Biofísica,
Faculdade de Medicina da Universidade de Coimbra, Pólo III
Azinhaga de Santa Comba, Celas
3000-548 Coimbra

Helena Donato
Documentation Department
Serviço de Documentação, Centro Hospitalar e Universitário de Coimbra
Praceta Prof. Mota Pinto
3000-075 Coimbra

Manuel Marques Ferreira
Institute of Endodontics
Instituto de Endodontia, Área de Medicina Dentária
Av. Bissaya Barreto, Bloco de Celas
3000-075 Coimbra

ACKNOWLEDGEMENTS

To Dr. Vitor Stuani, Faculdade de Odontologia de Bauru, for help in obtaining the articles full texts.

CONFLICTS OF INTEREST

The authors declare no conflict of interests.

FUNDING
None.

ABSTRACT

Objectives: To compare the treatments used to treat dentin hypersensitivity (DH), based on its efficacy and effect duration.

Methods: Medline/PubMed, Cochrane Library, EMBASE, and ClinicalTrials were searched for articles published between January 1st, 2008 and November 14th, 2018, in English, Portuguese or Spanish, reporting clinical trials, completed and with results. This systematic review protocol was registered in PROSPERO, number CRD42019121986.

Results: 74 randomized clinical trials were included in the systematic review, reporting patients from 16 to 65 years old, with a clinical diagnosis of DH, that evaluate the efficacy of a desensitizing product, compared to pre-treatment, used the evaporative method stimulation and the visual analogue scale. These studies evaluated 5366 patients and at least 9167 teeth. Seven follow-up periods were considered corresponding to an immediate, medium or long-time effect.

66 studies were included in the quantitative synthesis. Glutaraldehyde with HEMA, glass ionomer cements and Laser present significant immediate (until 7 days) DH reduction. Medium term (until 1 month) reduction was observed in stannous fluoride, glutaraldehyde with HEMA, hydroxyapatite, glass ionomer cements and Laser groups. Finally, long term significant reduction was seen at potassium nitrate, arginine, glutaraldehyde with HEMA, hydroxyapatite, adhesive systems, glass ionomer cements, and LASER.

Conclusions: All active ingredients show efficacy in DH reduction in different follow-up times. Only in-office treatments are effective in immediate DH reduction, maintaining its efficacy over time. For long time effects, at home treatments can also be used. More standardized evaluation protocols should be implemented to increase the robustly of the results.

Keywords: Dentin Sensitivity (MeSH); Dentin Hypersensitivity; Dentin Hypersensitivity treatments; Systematic Review (MeSH); Dentin desensitizing agent; Evidence-Based Dentistry (MeSH)

MAIN TEXT

BACKGROUND

Dentin hypersensitivity (DH) can be defined as "short and acute pain from exposed dentin in response to thermal, evaporative, tactile, osmotic, or chemical stimuli, and the same pain cannot be related to another defect or dental pathology".[1]

Despite being a widely studied theme, it remains a common problem in adults, with a prevalence ranging from 3% to 98%, for different included samples.[2] More accurately, Zeola *et al.* in a systematic review and meta-analysis published in 2019, conclude that the prevalence is between 11% and 33%.[3] At the same time, it is one of the dental pathologies most associated with pain and with lowest success in its treatment[4], thus justifying a detailed analysis of the available treatment methods.

Several theories have been proposed to explain the DH mechanism, with the hydrodynamic theory proposed by Brännström being the most accepted.[5] According to this theory, external stimuli such as thermal, mechanical, evaporative and osmotic, lead to the movement of fluid within the dentinal tubules and this movement indirectly stimulates the pulp nerve ends, causing a painful sensation. Therefore, for DH to occur, there must be two situations: dentin must be exposed, either by the loss of enamel or by a gingival recession, and the dentinal tubules must be permeable both to the oral cavity and to the pulp.[6]

DH treatment can be performed by several methods. In addition to the elimination of nociceptive stimuli, there are two main treatment strategies: modifying nervous response by preventing or reducing neuronal transmission and occluding the permeable dentinal tubules.[7] As nervous modifiers, potassium salts such as potassium fluoride, potassium chloride, and the most commonly used, potassium nitrate stand out.[8] Potassium alters the electrical potential of cells by depolarizing them. Because of this depolarization, there is a decrease in nervous excitability, and the cells are less responsive to stimuli.[9,10]

Regarding tubular occlusion, numerous active principles have been described, both chemical: fluorides[11], oxalates[12], or arginine[13,14] and physical: adhesives[15] or laser therapies.[16]

Fluorides indicated for DH treatment include sodium fluoride; silver diamide fluoride, tin fluoride, and amine fluoride. The application of fluorides creates a physical barrier since calcium fluoride is precipitated on the dentin surface.[11]

The oxalates occlude the dentinal tubules by reacting with calcium ions from the oral cavity, causing a precipitation reaction that leads to the formation of insoluble calcium oxalate crystals.[12]

Bioactive glasses, such as sodium, calcium phosphosilicate or calcium phosphate, promote the formation of apatite hydroxycarbonate, a mineral similar to hydroxyapatite, on the dentin surface, thus blocking the dentinal tubules.[7] Glutaraldehyde will react with serum albumin in the dentinal fluid, leading to the formation of precipitates and subsequent reduction of the diameter and blockade of the dentin tubules.[17] Arginine is an amino acid naturally found in saliva, and its combination with calcium carbonate reproduces the saliva's ability to occlude and seal dentinal tubules, resulting in a barrier resistant to acids and temperature dissolution.[13] Finally, strontium acts through the precipitation of particles on the dentin surface, thus preventing the movement of the dentinal fluid.[18]

Iontophoresis can be associated with other agents and can be used as a desensitizing treatment, since it transfers the active agent into the dentinal tubules through electrical pressure.[19–21] Physical agents such as resins, glass ionomer resins, and sealants, seal the dentinal tubules preventing the hydrodynamic stimulus to the pulp tissue.[7]

Lasers act via different mechanisms according to intensity. High-intensity lasers such as Nd: YAG, Er: YAG, Er, Cr: YSGG and CO2, are used to obliterate the dentinal tubules.[22] In contrast, low-intensity such as GaAlAs or He-Ne influence the reduction of pain symptoms, since they interfere with the Na^+ K^+ ion pump in the cell membrane, blocking the transmission of the pain stimulus.[23]

However, and despite the diversity of available treatments, there is still no consensus as to efficacy, so there is no treatment described as ideal.[24]

Thus, the objective of this systematic review is to compare the treatments used in dentin hypersensitivity, based on its efficacy and duration of action.

The aim was to carry out a systematic review of the literature with a quantitative comparison of the results in order to answer the following problem, intervention, comparison, and outcome (PICO) question: "Which desensitizing agent is the most effective in reducing DH in permanent teeth?" (Table 1).

METHODS

This systematic review was performed following the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines (http://www.prisma-statement.org) and the Cochrane Handbook of Systematic Reviews of Interventions (Version 5.1.0) (http://handbook-5-1.cochrane.org/).[25,26]

The protocol for this systematic review with meta-analysis was registered in PROSPERO with the number CRD42019121986.

Search strategy

The studies included in this systematic review were obtained from MEDLINE (accessed through PubMed), Cochrane Library, EMBASE and Clinical Trials databases.

The search strategy was in Medline: (#1 (dentin sensitivity[MeSH] NOT bleaching) AND treatment), in Cochrane Library (#1 MeSH descriptor: [Dentin Desensitizing Agents] explode all trees; #2 MeSH descriptor: [Dentin Sensitivity] explode all trees]) and EMBASE (#1 Entree descriptor: [Desensitizing Agent] explode all trees; #2 Entree descriptor: [Dentin Sensitivity] explode all trees]) and in Clinical Trials.gov: #1 (dentin hypersensitivity), using as filters publications between January 1st, 2008 and the November 14thof 2018, in English, Portuguese or Spanish and reporting clinical trials, completed and with results. Two reviewers (T.N. and M.P.) independently evaluated and selected the studies that met the inclusion criteria. A third reviewer (CM.M) was consulted where there was uncertainty regarding eligibility, and a decision arrived at by consensus.

Inclusion and exclusion criteria

For this systematic review, only clinical studies which met the following inclusion criteria were selected: (1) randomized clinical trials (RCT); (2) clinical diagnosis of DH; (3) assessment of the efficacy of a desensitizing product, reporting DH reduction compared to pre-treatment; (4) adulthood (16 to 65); (5) evaluation of DH through the evaporative method and (6) measurement of results using visual analogue scale (VAS) in cm (0-10) or mm (0-100). If the study has more than one follow-up all results were recorded.

Exclusion criteria were: (1) *in situ* studies; (2) post-surgical cases; (3) periodontal or bleaching post-treatment cases; (4) hypnosis; (5) post restoration/preparation clinical cases; (6) non-randomized clinical studies; (7) case reports; (8) reviews; and (9) comparison between active principles instead the baseline.

Data extraction

The studies that fulfilled the inclusion criteria were processed for the extraction of data. The data was recorded as follows: first author and year of publication, study design (parallel or split-mouth), type of treatment, number of teeth, number of subjects, mean age of patients or age range, gender, mean difference of pain and percentage of DH reduction, both between baseline and follow-up. In studies reporting drop-outs the final number of patients included in the analysis was recorded. Mean difference of pain and percentage of DH reduction was recorded from studies or calculated when enough data was available. These data were extracted from each study and grouped by different follow-ups and treatments. The different follow-up times were set to 1 day, from 2 to 7 days, from 8 to 15 days, from 15 to 30 days, from 1 to 6 months and more than 6 months. The information for assessment of the risk of bias was also performed. The extraction of the information was done by two independent authors using a standard form. A consensus meeting was always held to confirm the agreement and to resolve any disagreement between the reviewers.

Quality assessment

The evaluation of the methodological quality of the included studies is essential for understanding the results. This quality of each RCT study was assessed using the bias risk assessment tool described in the Cochrane Handbook of Systematic Reviews of Interventions (Version 5.1.0).[26] Briefly, six domains were evaluated: (1) random sequence generation to select the participants (selection bias); (2) allocation concealment (selection bias); (3) blinding intervention of participants and personnel (performance bias); (4) blinding of outcome assessment (detection bias); (5) incomplete outcome data (attrition bias); (6) selective reporting (reporting bias); and (7) other bias.

Quantitative analysis of follow-up

The quantitative analysis of the studies' results was carried out whenever it was possible to extract numerical data. The articles that stated no quantitative data in the text or in tables were excluded due to the difficulty of reading these values graphically, which led to the exclusion of 8 articles.[21,27–33] As in the systematic review, the results were grouped according to several follow-ups and treatments. In the analysis, the groups with less than two studies were excluded. In the extraction of data for statistical analysis the difference of the means or the medians and the respective standard error or standard deviation were considered.

Statistical analysis

The IBM® SPSS® Statistics software, version 24.0 (IBM Corporation, Armonk, New York, USA) was used. Non-parametric tests were used after confirming the existence of at least one of the following two conditions: (1) non-normal distribution (assessed by Shapiro-Wilk test) or (2) number of cases per group of less than 10.
For comparisons between two groups, the Mann-Whitney test was used. For comparisons of more than two groups, data were analyzed with the Kruskal-Wallis test. Multiple comparisons were made using the Tukey test. The level of significance was set at 0.05.

RESULTS

Study Characteristics

The PRISMA flow diagram of study selection is shown in Figure 1.

All included studies are RCT and use VAS and the evaporative stimulation method as a method of assessing dentine hypersensitivity. The variation of sample size is very large among the studies, with samples varying from 7 to 250 teeth.

Follow-up times were chosen according to the definition of therapeutic protocols, which may be immediate, medium-term and long-term. Most studies had more than one follow-up time, but most were immediate (up to 1 day) or medium-term (2 to 7 days, 8 to 15 days or 15 to 30 days). The long-term evaluation, with follow-up of 3 to 6 months or more than 6 months, was performed in a small minority of studies.

The treatments comprehended 24 active principles and a placebo group, as shown in Table 2 in accordance with the codification read in this article. The code 25 – others includes LED therapy and biomimetic mineralization system (BIMIN). The number of studies analyzed for each treatment are reported in the table 2.

Some were more represented in the literature, namely sodium fluoride, hydroxyapatite and laser. The placebo product used differs from study to study, and could be water, saline solution, glycerin, gel, sham treatments or no treatment. In the majority of studies there was a reduction of hypersensitivity in patients treated with the placebo group, with only 3 reporting no difference or a slight increase at some follow-ups.[4,34,35] Table 3 reports the results for different follow-ups.

In the studies included in this systematic review a total of 5366 patients and at least 9167 teeth were evaluated. Several studies reported only the number of subjects included but not the number of teeth, so it is possible that the sample is larger.

At 1 day of follow-up, all treatments promote a reduction in DH, ranging from 0.8% (arginine) to 62% (Laser). Glass ionomer cements, resins, adhesives and Lasers presented the best results, although some variations were found in Laser results (table 3.1). At the time of second and third follow-ups, from 2 to 7 days and from 8 to 15 days, respectively, high values were reported in NaF groups, hydroxyapatite and laser groups, with an increase in DH reduction seen consistently in all the groups (Tables 3.2 and 3.3). From 15 to 30 days, glutaraldehyde together with resins, adhesives, and Lasers presented the best results, with hydroxyapatite, arginine, and NaF also presenting a significant reduction in DH-associated pain (Table 3.4).

After 1 month and until 3 months, hydroxyapatite, resins, adhesives, glass ionomer cements, and lasers present several DH reductions above 80%, with all other treatments also presenting good results (Table 3.5).

For long-term evaluation, 3 to 6 months and more than 6 months, evaluation can only be made for some of the treatments due to a lack of studies. Hydroxyapatite, adhesives, glass ionomer cements and Lasers maintain a reduction of DH above 80% (Tables 3.6 and 3.7).

Some studies used associations of different treatments. As seen in table 3, these associated treatments usually result in an improvement of DH reduction, from about two times more.

Methodological quality assessment of included studies

The results of the quality assessment of RCTs of the systematic reviews can be seen in Appendix 1 and are schematically represented in Figure 2.

Only one study presented flaws in the methodological description of random sequence generation, while about 5.4% presented insufficient information. The allocation concealment was not always explained properly (9.5%) or was not performed (5.4%). However, most studies present randomization and allocation concealment, and are considered as having low risk of selection bias. Blinding intervention of participants and personnel in clinical procedures was impossible in several studies (32.4%) or was not explained in the description of the clinical study (8.1%). This performance bias was more common since the characteristics of products or techniques were easy to distinguish from each other. Blinding

evaluation of the results was possible in most studies, with minimal risk of bias (74.3%). Attrition bias with incomplete outcome data, and reporting bias were present in 10.8% of RCT studies, which had to be excluded from the quantitative analysis. Other biases were of minimal risk in all scrutinized studies.

Quantitative analysis of follow-up

The different follow-ups were analyzed separately, and the results can be observed in Table 4.

For immediate follow-up, less than 1 day, the general comparison between treatments showed statistically significant differences ($p < 0.0001$). The treatments with glutaraldehyde ($p < 0.001$), glass ionomer cements ($p < 0.05$) and lasers ($p < 0.01$) demonstrated statistically significant differences compared to placebo.

All the medium-term follow-ups showed significant differences between treatments. For the 2-to-7 days group, there were statistically significant differences between the various groups with $p = 0.007$. Compared to placebo, there were some treatments that significantly reduce the hypersensitivity such as glutaraldehyde ($p < 0.05$) and lasers ($p < 0.001$).

Similarly, for follow-up of 8 to 15 days, the general statistical differences between groups has a value of $p = 0.001$. However, a considerable number of studies were excluded with several treatments, namely: potassium chloride, amine fluoride, strontium acetate, iontophoresis, glutaraldehyde, strontium chloride, herbal, composite resins, dentin sealants, and potassium citrate. Nevertheless, the treatments analyzed showed a statistically significant reduction of hypersensitivity, namely stannous fluoride ($p < 0.05$), hydroxyapatite ($p < 0.05$), glass ionomer cements ($p < 0.01$) and lasers ($p < 0.001$).

At 15 to 30 days there were statistically significant differences in the general comparison between groups with $p = 0.001$. A decrease in hypersensitivity can be observed consistently in some groups, such as glutaraldehyde ($p < 0.001$), hydroxyapatite ($p < 0.01$), glass ionomer cements ($p < 0.01$) and lasers ($p < 0.001$).

In long-term follow-up times, it was only possible to analyze the treatments between 1 and 3 months, because for the other times there were not enough samples to make the comparison. In the follow-up of 1 to 3 months there were statistically significant differences in the general analysis between groups ($p < 0.0001$). Many treatments showed significant decreases relative to placebo such as potassium nitrate ($p < 0.01$), arginine ($p < 0.05$),

glutaraldehyde ($p < 0.01$), hydroxyapatite ($p < 0.001$), adhesive systems ($p < 0.05$), glass ionomer cements ($p < 0.01$) and lasers ($p < 0.001$).

Treatments with glutaraldehyde, lasers and glass ionomer cements present statistically significant differences relative to placebo at different follow-up times. However, when the results in the same group are compared over time, they have no differences, being treatments that effectively reduce sensitivity from the 1st day with consistent results over time. Other treatments demonstrated reduced hypersensitivity relative to placebo with statistical significance in medium-term follow-up. From 8 to 15 days in treatment with hydroxyapatite, there was a statistically significant reduction of hypersensitivity relative to placebo and increasing significance over time. The treatments with potassium nitrate revealed statistically significant differences in the reduction of hypersensitivity only in the follow-up of 1 to 3 months.

This analysis of the treatments' effect over time can be observed in Appendix 2. Statistically significant differences at different follow-up times were observed in the treatments with potassium nitrate and hydroxyapatite, as shown in Figures 3 and 4 respectively. The treatment with potassium nitrate demonstrates a significant reduction of hypersensitivity at the beginning of the intermediate follow-up time, between 2 and 7 days ($p < 0.01$), with a less pronounced decrease in the other medium-term follow-up times, returning to the values initially obtained at 3 months ($p < 0.001$).

Treatments with hydroxyapatite demonstrated a statistically significant efficacy in reducing hypersensitivity only from the 1st month ($p < 0.05$), which remains consistently up to 6 months ($p < 0.05$).

In laser treatments, there were no statistically significant differences over time in any follow-up between high and low power.

DISCUSSION

Dentin hypersensitivity is a clinical condition that interferes greatly with patients' quality of life, namely with daily tasks such as talking, drinking, eating and toothbrushing.[3] In a systematic review published by Douglas-de-Oliveira *et al.* in 2018, it was concluded that the treatments for dentin hypersensitivity result in a decrease in the physical symptoms of pain and an increase in the psychological dimension of comfort and consequently an improvement in several parameters of the quality of life, thus justifying the benefit of

performing clinical research in this field.[97] However, despite the great number of articles published, the methodologies used vary greatly among them. DH evaluation can be done using various stimuli, such as thermal, tactile or evaporative. For the present systematic review, only studies that performed DH stimulation through the evaporative method were considered. The choice was because it involves the stimulation of a greater area of dentin, it was the type of stimulus most commonly reported, since it is the most reproducible of the three, and it is also the most physiologically controllable.[24,75,98] Regarding the methods of evaluating DH, the VAS; Visual Rate Scale (VRS) and Schiff Cold Air Sensitivity Scale (SCASS), can be used. VAS consists of a straight line of 10 cm where the extremities are defined as "No pain" and "Severe pain". It is usually used from 0-10 cm or 0-100 mm.[99] The VAS evaluation was used in the present review since it is considered as an objective method to determine dentin pain[1], it is the most widely used method described in the literature, and allows us to obtain quantitative results. Studies which used other measurement instruments were not included in this review. Also, the fact that pain is subjective to each individual and each patient responds differently, as well as the fact that sometimes they do not understand the scales used, may have some impact on the results of the studies.

Interestingly, some studies reported significant DH reduction in groups absent from active principle[30,75,87,91,92,100], indicating the possible contribution of the placebo effect or even the Hawthorne effect on the action of desensitizers.[101] In the case of the placebo effect, the participants would present a physiological response after administration of an inert agent, such as saline solution. Regarding Hawthorne's effect, unpredictable results could be due to behavioral and emotional changes in the participants because they knew that they were taking part in a study or that they would be subject to observation by examiners.[102] The influence of these effects is difficult to calculate and should be considered. The existence of these placebo control groups may give additional information about the efficacy of the agents tested, allowing a better interpretation of the results; however, the use of negative controls in DH trials is controversial, since some authors support that, for ethical reasons, treatments without an active ingredient should not be performed. In some of the studies, positive control groups with fluoride dentifrices were used.[29,35,88,90,92,94,46,51,62–64,68,74,81] These pastes should not be used as a negative control, as stated by some authors, as they may have different fluorides or other agents, and it is not clear which fluoride concentration is effective in the treatment of DH.[1] As for the positive controls, since there is no gold standard treatment, their use is also controversial.[1]

Despite a Cochrane meta-analysis[103] reporting that there is no significant improvement with the use of potassium nitrate as a desensitizing agent, the present review shows that potassium nitrate is effective in the treatment of DH. All included studies of the different potassium salts reported a statistically significant treatment effect between the start of treatment and the last follow-up period, including in cases of association with other possible treatment agents. These differences between the present review and that of Poulsen *et al.* 2006 may be due to the studies included since we only included studies from 2008 on, the percentage of potassium in the agents used or methods of determination of DH reduction.

As mentioned, within the tubule occluders there are several options: bioactive glasses, fluorides, oxalates, iontophoresis, arginine, strontium, and glutaraldehyde. According to this systematic review, desensitizing agents that use sodium phosphosilicate calcium, calcium phosphate or nano-hydroxyapatite contribute to the improvement of the symptoms of DH. As regards sodium and calcium phosphosilicate, the results of this study corroborate the results of the review by Zhu *et al.*[104], since they present a statistically significant treatment effect in all included studies.

In the present review, several fluorides were found for DH treatment, namely sodium fluoride, silver diamide fluoride, tin fluoride, and amine fluoride. Because it is commonly used in clinical practice, as previously stated, sodium fluoride was mostly used as a negative and/or positive control; however, all studies reported a decrease of DH with its use. The efficacy of DH reduction by fluoride action is supported by its mechanism of action, with formation of precipitated and dentinal tubule occlusion.[105] Also, in the remaining fluorides, all studies revealed the significance of treatment effect values.

Desensitizing agents that use oxalates improve the symptomatology of DH, revealing a statistically significant treatment effect in all studies included in this systematic review. These results do not meet the meta-analysis of Cunha-Cruz *et al.*, which states that there is no benefit in the use of oxalates for the treatment of DH[106], but again the inclusion of different studies and study methodology can support this difference.

Arginine-based dentifrices have also been used as desensitizers with positive results in more than one systematic review.[107,108] The results of this review show that there are significant improvements in DH when treated with arginine-based products, but only with statistical significance in 1 to 3 months follow-up.

Strontium in the form of strontium acetate or strontium chloride may be an effective method of DH treatment, but the statistical analysis was not performed due to an insufficient number of studies.[54,59,68,79,85]

In vitro studies have shown that the *Spinacia oleracia* agent is effective in the occlusion of dentinal tubules through the formation of calcium oxalate crystals. In this review, 3 studies were included that refer to a statistical improvement in DH with the use of herbal dentifrices, two of which refer to the agent *Spinacia oleracea.*[79,92,93] However, the presence of potassium nitrate in the composition of the described dentifrices does not allow a correct understanding of the true nature of the desensitizing effect of *Spinacia oleracia* in the treatment of DH, since this effect may be due to the nitrate in the composition of the product.

A study by Azarpazhooh *et al.*, which uses ozone to treat DH, shows a statistically significant improvement in DH.[87] However, the true effect of ozone can be difficult to determine, since these results may have been achieved through a vacuum effect that will lead to the dissection and evaporation of the more superficial dentinal fluid. This dissection results in the deposition of salts in the dentinal tubules that lead to its filling, thus causing a relief in the symptomatology.[87]

Regarding physical agents, the use of lasers has been increasing in the dentistry field and DH treatment is no exception, being described first by Matsumoto *et al.*[109] There are several systematic reviews and meta-analyses that report that lasers are effective in the treatment of DH[22,110,111], which is in agreement with the results we obtained.

One of the major limitations of the studies included in this review is that many have a short follow-up. In clinical practice, when patients seek treatment for DH, they seek long-term results, so follow-up times should last until the agent used has the maximum effect to reduce the placebo effect mentioned above. Another problem is the small number of studies in some of the categories presented, which means that the sample included in some groups is reduced, limiting the conclusions obtained. Although parameters such as DH assessment and stimulus type were chosen to decrease heterogeneity, this is also a major limitation since there are different study designs (parallel or split-mouth) and different follow-ups in the studies selected for this review. This heterogeneity is most noticeable in studies involving lasers, due to different types of lasers used, time of exposition or energy used.

Even though we chose the evaporative method analyzed with the VAS that guaranteed an objective and quantitative analysis, we thought that some recommendations for future studies would be important:

1. Age stratification of the sample should be performed since some studies reported included individuals ranging from 18 to 65/70 years old. Since the incidence of HD varies greatly with age, besides other factors, more homogenous age samples should be evaluated.
2. The spilt-mouth design should be chosen wherever possible since it allows to evaluate the response to HD treatment in the same individual. In situations were split-mouth design cannot be performed, such as dentifrices evaluation, a control group should always be included.
3. Control groups with placebo should be performed in all studies since the published results show a decrease in HD attributed to a placebo effect. The chosen placebo should be adapted to the evaluated treatment. In a situation as laser or iontophoresis, the placebo should be performed with the treatment simulation. In chemical agents, the placebo should be chosen accordingly the pharmaceutical formulation: glycerin gel or saline solution should be used as a placebo where gel formulations or liquid formulations are tested, respectively.
4. HD evaluation should be performed with the evaporative method, since it gives the most accurate results, for the reasons stated above. The distance between the air spray and dental structure, the air spray pressure, and the test duration should be standardized. After isolation of the adjacent teeth, the air syringe should be placed 2-3 mm from the tooth surface, at a perpendicular position of 90º, and a continuous air blast of 45 to 60 psi should be applied for 2 to 3 seconds. The air temperature should be around 20º C (19-22ºC).
5. Combined evaluation with 2 methods can be used, as the evaporative and tactile method, since it gives a more accurate result. The results of the methods should be reported separately, and a combined score should also be included.
6. VAS should be used to evaluate the HD reduction since it gives a quantitative result. Combined evaluation with other scales can be performed, but again, results should be reported separately and in a combined score.
7. Studies should include follow-ups that allow evaluating the immediate, medium and long-term effect of the treatment in the same sample. HD evaluation should be performed at 1 day, 1 week, 1 month, 3 months and 6 months.

We believe that these factors may influence the test results and to obtain further clinical evidence about the effects of the treatments on hypersensitivity it would be advisable to standardize them.

CONCLUSION

The results of the present review demonstrate positive levels of efficacy in all treatment options for DH reduction, irrespective of the mechanism of action.

With the accomplishment of this systematic review and quantitative analysis of follow-up, the most effective agent in the treatment of DH was determined. In office treatments both chemical as glutaraldehyde with HEMA, or physical as glass ionomer cements or Laser are effective in immediate reduction of DH associated pain, maintaining its efficacy over time. For long time effects, at home treatments with chemical agents, such as potassium nitrate, arginine or hydroxyapatite can also be used to treat DH with significant results.

In the treatment of dentin hypersensitivity, in addition to the appropriate choice of desensitizing agent, it is important to evaluate the predisposing factors [112]. This evaluation is fundamental to assess the risk of exposure of dentin tissue by enamel removal, as occurs in patients with very acidic diets, for example. A therapy with a desensitizing agent, as a minimally invasive, cost-effective, and safe treatment is also reversible, and therefore the result is dependent on the removal of the causative agent.

In order to understand the best option among the different groups, a greater homogeneity of the methodology of the studies of this area would be necessary.

REFERENCES

1. Holland GR, Narhi MN, Addy M, Gangarosa L, Orchardson R. Guidelines for the design and conduct of clinical trials on dentine hypersensitivity. *J Clin Periodontol*. 1997;24(11):808-813.
2. Splieth CH, Tachou A. Epidemiology of dentin hypersensitivity. *Clin Oral Investig*. 2013;17 Suppl 1(S1):S3-8.
3. Favaro Zeola L, Soares PV, Cunha-Cruz J. Prevalence of dentin hypersensitivity: Systematic review and meta-analysis. *J Dent*. 2019;81:1-6.
4. Idon PI, Esan TA, Bamise CT. Efficacy of Three In-Office Dentin Hypersensitivity Treatments. *Oral Health Prev Dent*. 2017;15(3):207-214.
5. Brannstrom M. Dentin sensitivity and aspiration of odontoblasts. *J Am Dent Assoc*. 1963;66:366-370.
6. Canadian Advisory Board on Dentin Hypersensitivity. Consensus-based recommendations for the diagnosis and management of dentin hypersensitivity. *J Can Dent Assoc*. 2003;69(4):221-226.

7. Shiau H. Dentin hypersensitivity. *J Evid Based Dent Pract*. 2012;12(3 Suppl):220-228.
8. Hong JY, Lim HC, Herr Y. Effects of a mouthwash containing potassium nitrate, sodium fluoride, and cetylpyridinium chloride on dentin hypersensitivity: a randomized, double-blind, placebo-controlled study. *J Periodontal Implant Sci*. 2016;46(1):46-56.
9. Markowitz K, Bilotto G, Kim S. Decreasing intradental nerve activity in the cat with potassium and divalent cations. *Arch Oral Biol*. 1991;36(1):1-7.
10. Orchardson R, Gillam DG. The efficacy of potassium salts as agents for treating dentin hypersensitivity. *J Orofac Pain*. 2000;14(1):9-19.
11. Petersson LG. The role of fluoride in the preventive management of dentin hypersensitivity and root caries. *Clin Oral Investig*. 2013;17 Suppl 1(Suppl 1):S63-71.
12. Arnold WH, Prange M, Naumova EA. Effectiveness of various toothpastes on dentine tubule occlusion. *J Dent*. 2015;43(4):440-449.
13. Petrou I, Heu R, Stranick M, et al. A breakthrough therapy for dentin hypersensitivity: how dental products containing 8% arginine and calcium carbonate work to deliver effective relief of sensitive teeth. *J Clin Dent*. 2009;20(1):23-31.
14. Yang ZY, Wang F, Lu K, Li YH, Zhou Z. Arginine-containing desensitizing toothpaste for the treatment of dentin hypersensitivity: a meta-analysis. *Clin Cosmet Investig Dent*. 2016;8:1-14.
15. Kathariya R. Dental hypersensitivity: A common cold in dentistry. *J Dent Res Rev*. 2016;3(2):49.
16. Kimura Y, Wilder-Smith P, Yonaga K, Matsumoto K. Treatment of dentine hypersensitivity by lasers: a review. *J Clin Periodontol*. 2000;27(10):715-721.
17. Ishihata H, Finger WJ, Kanehira M, Shimauchi H, Komatsu M. In vitro dentin permeability after application of Gluma® desensitizer as aqueous solution or aqueous fumed silica dispersion. *J Appl Oral Sci*. 2011;19(2):147-153.
18. Van Loveren C, Schmidlin PR, Martens LC, Amaechi BT. Dentin hypersensitivity management. *Clin Dent Rev*. 2018;2(1):6.
19. Patil AR, Varma S, Suragimath G, Abbayya K, Zope SA, Kale V. Comparative Evaluation of Efficacy of Iontophoresis with 0.33% Sodium Fluoride Gel and Diode Laser Alone on Occlusion of Dentinal Tubules. *J Clin Diagn Res*. 2017;11(8):ZC123-ZC126.
20. Brahmbhatt N, Bhavsar N, Sahayata V, Acharya A, Kshatriya P. A double blind controlled trial comparing three treatment modalities for dentin hypersensitivity. *Med Oral Patol Oral Cir Bucal*. 2012;17(3):e483-90.
21. Kumar S, Thomas BS, Gupta K, Guddattu V, Alexander M. Iontophoresis and topical application of 8% arginine-calcium carbonate to treat dentinal hypersensitivity. *Niger J Clin Pract*. 2018;21(8):1029-1033.

22. Machado AC, Viana ÍEL, Farias-Neto AM, et al. Is photobiomodulation (PBM) effective for the treatment of dentin hypersensitivity? A systematic review. *Lasers Med Sci*. 2018;33(4):745-753.
23. Orchardson R, Peacock JM, Whitters CJ. Effect of pulsed Nd:YAG laser radiation on action potential conduction in isolated mammalian spinal nerves. *Lasers Surg Med*. 1997;21(2):142-148.
24. Lin PY, Cheng YW, Chu CY, Chien KL, Lin CP, Tu YK. In-office treatment for dentin hypersensitivity: a systematic review and network meta-analysis. *J Clin Periodontol*. 2013;40(1):53-64.
25. Liberati A. The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration. *Ann Intern Med*. 2009;151(4):W.
26. Carvalho A, Silva V, Grande A. Avaliação do risco de viés de ensaios clínicos randomizados pela ferramenta da colaboração Cochrane. *Diagn Trat*. 2013;18(1):38-44.
27. Ding YJ, Yao H, Wang GH, Song H. A randomized double-blind placebo-controlled study of the efficacy of Clinpro XT varnish and Gluma dentin desensitizer on dentin hypersensitivity. *Am J Dent*. 2014;27(2):79-83.
28. Konekeri V, Bennadi D, Manjunath M, Kshetrimayum N, Siluvai S, Reddy CVK. A Clinical Study to assess the Effectiveness of CPPACP (Casein Phosphopeptide-Amorphous calcium phosphate) versus Potassium-nitrate (KNO3) on cervical dentine hypersensitivity. *J Young Pharm*. 2015;7(3):217-224.
29. Lopes AO, Aranha ACC. Comparative evaluation of the effects of Nd:YAG laser and a desensitizer agent on the treatment of dentin hypersensitivity: a clinical study. *Photomed Laser Surg*. 2013;31(3):132-138.
30. Mehta D, Gowda VS, Santosh A, Finger WJ, Sasaki K. Randomized controlled clinical trial on the efficacy of dentin desensitizing agents. *Acta Odontol Scand*. 2014;72(8):936-941.
31. Mehta D, Gowda V, Finger WJ, Sasaki K. Randomized, placebo-controlled study of the efficacy of a calcium phosphate containing paste on dentin hypersensitivity. *Dent Mater*. 2015;31(11):1298-1303.
32. Raichur PS, Setty SB, Thakur SL. Comparative evaluation of diode laser, stannous fluoride gel, and potassium nitrate gel in the treatment of dentinal hypersensitivity. *Gen Dent*. 2013;61(3):66-71.
33. Zang P, Parkinson C, Hall C, et al. A Randomized Clinical Trial Investigating the Effect of Particle Size of Calcium Sodium Phosphosilicate (CSPS) on the Efficacy of CSPS-containing Dentifrices for the Relief of Dentin Hypersensitivity. *J Clin Dent*.

2016;27(2):54-60.
34. Litkowski L, Greenspan DC. A clinical study of the effect of calcium sodium phosphosilicate on dentin hypersensitivity--proof of principle. *J Clin Dent*. 2010;21(3):77-81.
35. Bal MV, Keskiner İ, Sezer U, Açıkel C, Saygun I. Comparison of Low Level Laser and Arginine-Calcium Carbonate Alone or Combination in the Treatment of Dentin Hypersensitivity: A Randomized Split-Mouth Clinical Study. *Photomed Laser Surg*. 2015;33(4):200-205.
36. Ozen T, Orhan K, Avsever H, Tunca YM, Ulker AE, Akyol M. Dentin hypersensitivity: a randomized clinical comparison of three different agents in a short-term treatment period. *Oper Dent*. 2009;34(4):392-398.
37. Yilmaz H, Kurtulmus-Yilmaz S, Cengiz E. Long-term effect of diode laser irradiation compared to sodium fluoride varnish in the treatment of dentine hypersensitivity in periodontal maintenance patients: a randomized controlled clinical study. *Photomed Laser Surg*. 2011;29(11):721-725.
38. Vora J, Mehta D, Meena N, Sushma G, Finger WJ, Kanehira M. Effects of two topical desensitizing agents and placebo on dentin hypersensitivity. *Am J Dent*. 2012;25(5):293-298.
39. Orhan K, Aksoy U, Can-Karabulut DC, Kalender A. Low-level laser therapy of dentin hypersensitivity: a short-term clinical trial. *Lasers Med Sci*. 2011;26(5):591-598.
40. Aranha ACC, Eduardo CdeP. Effects of Er:YAG and Er,Cr:YSGG lasers on dentine hypersensitivity. Short-term clinical evaluation. *Lasers Med Sci*. 2012;27(4):813-818.
41. Yilmaz HG, Kurtulmus-Yilmaz S, Cengiz E, Bayindir H, Aykac Y. Clinical evaluation of Er,Cr:YSGG and GaAlAs laser therapy for treating dentine hypersensitivity: A randomized controlled clinical trial. *J Dent*. 2011;39(3):249-254.
42. Yilmaz H, Cengiz E, Kurtulmus-Yilmaz S, Leblebicioglu B. Effectiveness of Er,Cr:YSGG laser on dentine hypersensitivity: a controlled clinical trial. *J Clin Periodontol*. 2011;38(4):341-346.
43. Dilsiz A, Aydin T, Canakci V, Gungormus M. Clinical evaluation of Er:YAG, Nd:YAG, and diode laser therapy for desensitization of teeth with gingival recession. *Photomed Laser Surg*. 2010;28 Suppl 2(S2):S11-7.
44. Hoang-Dao BT, Hoang-Tu H, Tran-Thi NN, Koubi G, Camps J, About I. Clinical efficiency of a natural resin fluoride varnish (Shellac F) in reducing dentin hypersensitivity. *J Oral Rehabil*. 2009;36(2):124-131.
45. França IL, Sallum EA, Do Vale HF, Casati MZ, Sallum AW, Stewart B. Efficacy of a combined in-office/home-use desensitizing system containing 8% arginine and calcium carbonate in reducing dentin hypersensitivity: an 8-week randomized clinical

study. *Am J Dent*. 2015;28(1):45-50.

46. Dilsiz A, Aydın T, Emrem G. Effects of the combined desensitizing dentifrice and diode laser therapy in the treatment of desensitization of teeth with gingival recession. *Photomed Laser Surg*. 2010;28 Suppl 2(S2):S69-74.
47. Osmari D, Fraga S, Ferreira ACO, Eduardo CP, Marquezan M, Silveira BLD. In-office Treatments for Dentin Hypersensitivity: A Randomized Split-mouth Clinical Trial. *Oral Health Prev Dent*. 2018;16(2):125-130.
48. Soares MDL, Porciúncula GB, Lucena MIHM De, Gueiros LAM, Leão JC, Carvalho ADAT. Efficacy of Nd:YAG and GaAlAs lasers in comparison to 2% fluoride gel for the treatment of dentinal hypersensitivity. *Gen Dent*. 2016;64(6):66-70.
49. Ravishankar P, Viswanath V, Archana D, Keerthi V, Dhanapal S, Lavanya Priya K. The effect of three desensitizing agents on dentin hypersensitivity: A randomized, split-mouth clinical trial. *Indian J Dent Res*. 2018;29(1):51.
50. Pinna R, Bortone A, Sotgiu G, Dore S, Usai P, Milia E. Clinical evaluation of the efficacy of one self-adhesive composite in dental hypersensitivity. *Clin Oral Investig*. 2015;19(7):1663-1672.
51. Femiano F, Femiano R, Lanza A, Festa MV, Rullo R, Perillo L. Efficacy of diode laser in association to sodium fluoride vs Gluma desensitizer on treatment of cervical dentin hypersensitivity. A double blind controlled trial. *Am J Dent*. 2013;26(4):214-218.
52. Kara C, Orbak R. Comparative evaluation of Nd:YAG laser and fluoride varnish for the treatment of dentinal hypersensitivity. *J Endod*. 2009;35(7):971-974.
53. Torres C, Silva T, Fonseca B, et al. The Effect of Three Desensitizing Agents on Dentin Hypersensitivity: A Randomized, Split-mouth Clinical Trial. *Oper Dent*. 2014;39(5):E186-E194.
54. Seong J, Parkinson CP, Davies M, Claydon NCA, West NX. Randomised clinical trial to evaluate changes in dentine tubule occlusion following 4 weeks use of an occluding toothpaste. *Clin Oral Investig*. 2018;22(1):225-233.
55. He T, Barker M, Qaqish J, Sharma N. Fast onset sensitivity relief of a 0.454% stannous fluoride dentifrice. *J Clin Dent*. 2011;22(2):46-50.
56. Mason S, Hughes N, Sufi F, et al. A comparative clinical study investigating the efficacy of a dentifrice containing 8% strontium acetate and 1040 ppm fluoride in a silica base and a control dentifrice containing 1450 ppm fluoride in a silica base to provide immediate relief of dentin hypersensitivity. *J Clin Dent*. 2010;21(2):42-48.
57. Parkinson CR, Hughes N, Hall C, Whelton H, Gallob J, Mason S. Three randomized clinical trials to assess the short-term efficacy of anhydrous 0.454% w/w stannous fluoride dentifrices for the relief of dentin hypersensitivity. *Am J Dent*. 2016;29(1):25-32.

58. He T, Cheng R, Biesbrock AR, Chang A, Sun L. Rapid desensitizing efficacy of a stannous-containing sodium fluoride dentifrice. *J Clin Dent*. 2011;22(2):40-45.
59. West N, Newcombe RG, Hughes N, et al. A 3-day randomised clinical study investigating the efficacy of two toothpastes, designed to occlude dentine tubules, for the treatment of dentine hypersensitivity. *J Dent*. 2013;41(2):187-194.
60. Erdemir U, Yildiz E, Kilic I, Yucel T, Ozel S. The efficacy of three desensitizing agents used to treat dentin hypersensitivity. *J Am Dent Assoc*. 2010;141(3):285-296.
61. Talesara K, Kulloli A, Shetty S, Kathariya R. Evaluation of potassium binoxalate gel and Nd:YAG laser in the management of dentinal hypersensitivity: a split-mouth clinical and ESEM study. *Lasers Med Sci*. 2014;29(1):61-68.
62. Patil SA, Naik BD, Suma R. Evaluation of three different agents for in-office treatment of dentinal hypersensitivity: a controlled clinical study. *Indian J Dent Res*. 2015;26(1):38-42.
63. Lopes AO, de Paula EC, Aranha ACC. Evaluation of different treatment protocols for dentin hypersensitivity: an 18-month randomized clinical trial. *Lasers Med Sci*. 2017;32(5):1023-1030.
64. Lopes AO, de Paula EC, Aranha ACC. Clinical evaluation of low-power laser and a desensitizing agent on dentin hypersensitivity. *Lasers Med Sci*. 2015;30(2):823-829.
65. Sethna GD, Prabhuji ML V, Karthikeyan B V. Comparison of two different forms of varnishes in the treatment of dentine hypersensitivity: a subject-blind randomised clinical study. *Oral Health Prev Dent*. 2011;9(2):143-150.
66. Canali GD, Ignacio SA, Rached RN, Souza EM. Clinical efficacy of resin-based materials for dentin hypersensitivity treatment. *Am J Dent*. 2017;30(4):201-204.
67. Madruga MM, Silva AF, Rosa WL, Piva E, Lund RG. Evaluation of dentin hypersensitivity treatment with glass ionomer cements: A randomized clinical trial. *Braz Oral Res*. 2017;31:e3.
68. Antoniazzi RP, Machado ME, Grellmann AP, Santos RCV, Zanatta FB. Effectiveness of a desensitizing agent for topical and home use for dentin hypersensitivity: a randomized clinical trial. *Am J Dent*. 2014;27(5):251-257.
69. Tirapelli C, Panzeri H, Lara EHG, Soares RG, Peitl O, Zanotto ED. The effect of a novel crystallised bioactive glass-ceramic powder on dentine hypersensitivity: a long-term clinical study. *J Oral Rehabil*. 2011;38(4):253-262.
70. Jalali Y, Lindh L. A randomized prospective clinical evaluation of two desensitizing agents on cervical dentine sensitivity. A pilot study. *Swed Dent J*. 2010;34(2):79-86.
71. Dantas EM, Amorim FK, Nóbrega FJ, Dantas PMC, Vasconcelos RG, Queiroz LMG. Clinical Efficacy of Fluoride Varnish and Low-Level Laser Radiation in Treating Dentin Hypersensitivity. *Braz Dent J*. 2016;27(1):79-82.

72. Hall C, Mason S, Cooke J. Exploratory randomised controlled clinical study to evaluate the comparative efficacy of two occluding toothpastes - a 5% calcium sodium phosphosilicate toothpaste and an 8% arginine/calcium carbonate toothpaste - for the longer-term relief of dentine hypersensitivity. *J Dent*. 2017;60:36-43.
73. Guentsch A, Seidler K, Nietzsche S, et al. Biomimetic mineralization: long-term observations in patients with dentin sensitivity. *Dent Mater*. 2012;28(4):457-464.
74. Han KH, Hong JH, Shin JH, Lee JY, Shin SW. Effects of desensitizing agents for cervical dentin hypersensitivity: A randomized clinical trial. *Am J Dent*. 2017;30(2):84-88.
75. Pradeep A, Sharma A. Comparison of Clinical Efficacy of a Dentifrice Containing Calcium Sodium Phosphosilicate to a Dentifrice Containing Potassium Nitrate and to a Placebo on Dentinal Hypersensitivity: A Randomized Clinical Trial. *J Periodontol*. 2010;81(8):1167-1173.
76. Vano M, Derchi G, Barone A, Covani U. Effectiveness of nano-hydroxyapatite toothpaste in reducing dentin hypersensitivity: a double-blind randomized controlled trial. *Quintessence Int*. 2014;45(8):703-711.
77. Vano M, Derchi G, Barone A, Pinna R, Usai P, Covani U. Reducing dentine hypersensitivity with nano-hydroxyapatite toothpaste: a double-blind randomized controlled trial. *Clin Oral Investig*. 2018;22(1):313-320.
78. Du Min Q, Bian Z, Jiang H, et al. Clinical evaluation of a dentifrice containing calcium sodium phosphosilicate (novamin) for the treatment of dentin hypersensitivity. *Am J Dent*. 2008;21(4):210-214.
79. Majji P, Murthy KRV. Clinical efficacy of four interventions in the reduction of dentinal hypersensitivity: A 2-month study. *Indian J Dent Res*. 2016;27(5):477-482.
80. Katanec T, Majstorovic M, Negovetic Vranic D, Ivic Kardum M, Marks LA. New toothpaste to deal with dentine hypersensitivity: double-blind randomized controlled clinical trial. *Int J Dent Hyg*. 2016;16(1):78-84.
81. Sharma D, McGuire JA, Gallob JT, Amini P. Randomised clinical efficacy trial of potassium oxalate mouthrinse in relieving dentinal sensitivity. *J Dent*. 2013;41 Suppl 4:S40-8.
82. Salian S, Thakur S, Kulkarni S, LaTorre G. A randomized controlled clinical study evaluating the efficacy of two desensitizing dentifrices. *J Clin Dent*. 2010;21(3):82-87.
83. Sharma N, Roy S, Kakar A, Greenspan DC, Scott R. A clinical study comparing oral formulations containing 7.5% calcium sodium phosphosilicate (NovaMin), 5% potassium nitrate, and 0.4% stannous fluoride for the management of dentin hypersensitivity. *J Clin Dent*. 2010;21(3):88-92.
84. Gibson M, Sharif MO, Smith A, Saini P, Brunton PA. A practice-based randomised

controlled trial of the efficacy of three interventions to reduce dentinal hypersensitivity. *J Dent*. 2013;41(8):668-674.

85. Hughes N, Mason S, Jeffery P, et al. A comparative clinical study investigating the efficacy of a test dentifrice containing 8% strontium acetate and 1040 ppm sodium fluoride versus a marketed control dentifrice containing 8% arginine, calcium carbonate, and 1450 ppm sodium monofluorophosphate in reducing dentinal hypersensitivity. *J Clin Dent*. 2010;21(2):49-55.
86. Ko Y, Park J, Kim C, Park J, Baek SH, Kook YA. Treatment of dentin hypersensitivity with a low-level laser-emitting toothbrush: double-blind randomised clinical trial of efficacy and safety. *J Oral Rehabil*. 2014;41(7):523-531.
87. Azarpazhooh A, Limeback H, Lawrence HP, Fillery ED. Evaluating the effect of an ozone delivery system on the reversal of dentin hypersensitivity: a randomized, double-blinded clinical trial. *J Endod*. 2009;35(1):1-9.
88. Wang L, Magalhães AC, Francisconi-Dos-Rios LF, et al. Treatment of Dentin Hypersensitivity Using Nano-Hydroxyapatite Pastes: A Randomized Three-Month Clinical Trial. *Oper Dent*. 2016;41(4):E93-E101.
89. Parkinson CR, Jeffery P, Milleman JL, Milleman KR, Mason S. Confirmation of efficacy in providing relief from the pain of dentin hypersensitivity of an anhydrous dentifrice containing 0.454% with or without stannous fluoride in an 8-week randomized clinical trial. *Am J Dent*. 2015;28(4):190-196.
90. Young S, Sufi F, Siddiqi M, Maclure R, Holt J. A Randomized Non-Inferiority Clinical Study to Evaluate the Efficacy of Two Dentifrices for Dentin Hypersensitivity. *J Clin Dent*. 2016;27(4):97-104.
91. Pradeep AR, Agarwal E, Naik SB, Bajaj P, Kalra N. Comparison of efficacy of three commercially available dentifrices [corrected] on dentinal hypersensitivity: a randomized clinical trial. *Aust Dent J*. 2012;57(4):429-434.
92. Kumari M, Naik SB, Martande SS, Pradeep AR, Singh P. Comparative efficacy of a herbal and a non-herbal dentifrice on dentinal hypersensitivity: a randomized, controlled clinical trial. *J Investig Clin Dent*. 2016;7(1):46-52.
93. Kumari M, Naik S, Rao N, Martande S, Pradeep A. Clinical efficacy of a herbal dentifrice on dentinal hypersensitivity: a randomized controlled clinical trial. *Aust Dent J*. 2013;58(4):483-490.
94. Amaechi BT, Lemke KC, Saha S, Gelfond J. Clinical Efficacy in Relieving Dentin Hypersensitivity of Nanohydroxyapatite-containing Cream: A Randomized Controlled Trial. *Open Dent J*. 2018;12:572-585.
95. Kashyap R, Hedge S, Arun Kumar MS, Shetty DG. Evaluation of the efficacy of a 5% calcium sodium phosphosilicate (Novamin) containing dentifrice for the relief of

dentinal hypersensitivity: a clinical study. *Indian J Dent Res*. 2012;23(3):363-367.
96. Ehlers V, Ernst C-P, Reich M, Kämmerer P, Willershausen B. Clinical comparison of gluma and Er:YAG laser treatment of cervically exposed hypersensitive dentin. *Am J Dent*. 2012;25(3):131-135.
97. Douglas-de-Oliveira DW, Vitor GP, Silveira JO, Martins CC, Costa FO, Cota LOM. Effect of dentin hypersensitivity treatment on oral health related quality of life — A systematic review and meta-analysis. *J Dent*. 2018;71:1-8.
98. Ide M, Wilson RF, Ashley FP. The reproducibility of methods of assessment for cervical dentine hypersensitivity. *J Clin Periodontol*. 2001;28(1):16-22.
99. Hu ML, Zheng G, Zhang YD, Yan X, Li XC, Lin H. Effect of desensitizing toothpastes on dentine hypersensitivity: A systematic review and meta-analysis. *J Dent*. 2018;75:12-21.
100. Shetty S, Kohad R, Yeltiwar R. Hydroxyapatite as an in-office agent for tooth hypersensitivity: a clinical and scanning electron microscopic study. *J Periodontol*. 2010;81(12):1781-1789.
101. Molina A, García-Gargallo M, Montero E, Tobías A, Sanz M, Martín C. Clinical efficacy of desensitizing mouthwashes for the control of dentin hypersensitivity and root sensitivity: a systematic review and meta-analysis. *Int J Dent Hyg*. 2017;15(2):84-94.
102. McCambridge J, Witton J, Elbourne DR. Systematic review of the Hawthorne effect: new concepts are needed to study research participation effects. *J Clin Epidemiol*. 2014;67(3):267-277.
103. Poulsen S, Errboe M, Lescay Mevil Y, Glenny A-M. Potassium containing toothpastes for dentine hypersensitivity. *Cochrane Database Syst Rev*. 2006;(3):CD001476.
104. Zhu M, Li J, Chen B, et al. The Effect of Calcium Sodium Phosphosilicate on Dentin Hypersensitivity: A Systematic Review and Meta-Analysis. Milgrom PM, ed. *PLoS One*. 2015;10(11):e0140176.
105. Davari A, Ataei E, Assarzadeh H. Dentin hypersensitivity: etiology, diagnosis and treatment; a literature review. *J Dent (Shiraz, Iran)*. 2013;14(3):136-145.
106. Cunha-Cruz J, Stout JR, Heaton LJ, Wataha JC, Northwest PRECEDENT. Dentin Hypersensitivity and Oxalates. *J Dent Res*. 2011;90(3):304-310.
107. Sharif MO, Iram S, Brunton PA. Effectiveness of arginine-containing toothpastes in treating dentine hypersensitivity: a systematic review. *J Dent*. 2013;41(6):483-492.
108. Magno MB, Nascimento GCR, Da Penha NKS, Pessoa OF, Loretto SC, Maia LC. Difference in effectiveness between strontium acetate and arginine-based toothpastes to relieve dentin hypersensitivity. A systematic review. *Am J Dent*. 2015;28(1):40-44.
109. Matsumoto K, Funai H, Shirasuka T, Wakabayashi H. Effects of Nd:YAG laser in

treatment of cervical hypersensitive dentin. *Japanese J Conserv Dent*. 1985;28:760-765.

110. Sgolastra F, Petrucci A, Severino M, Gatto R, Monaco A. Lasers for the Treatment of Dentin Hypersensitivity. *J Dent Res*. 2013;92(6):492-499.
111. He S, Wang Y, Li X, Hu D. Effectiveness of laser therapy and topical desensitising agents in treating dentine hypersensitivity: a systematic review. *J Oral Rehabil*. 2011;38(5):348-358.
112. Shiau HJ. Dentin Hypersensitivity. *J Evid Based Dent Pract*. 2012;12(3):220-228.

Tables legends

Table 1 – Schematic representation of PICO question

Table 2 – Codification and number of studies included for each treatment

Table 3 - 3.1 - Summary of the included studies on the systematic review up to 1 day; **3.2** - from 2 to 7 days; **3.3** - from 8 to 15 days; **3.4**- from 15 to 30 days; **3.5** - from 1 to 3 months; **3.6** - from 3 to 6 months and **3.7** - more than 6 months.

Table 4 – *P* values referent to the statistical comparison between DH reduction of each treatment *versus* the placebo at the different time points

Table 1 – Schematic representation of PICO question

Population / Problem	Adult patients with DH
Intervention	Desensitizing Treatments
Comparison	Placebo or No treatment
Outcome	Pain Reduction

Table 2 – Codification and number of studies included for each treatment

Code	*Treatment*	*Number of studies*
1	Placebo	24
2	Potassium nitrate	17
3	Potassium chloride	1
4	Potassium fluoride	1
5	Sodium fluoride (NaF)	33
6	Stannous fluoride	6
7	Amine fluoride	1
8	Strontium acetate	4
9	Oxalates	9
10	Iontophoresis	2
11	Arginine	12
12	Glutaraldehyde + HEMA	18
13	Chlorhexidine	1
14	Strontium Chloride	3
15	Hydroxyapatite	20
16	Herbal	3
17	Ozone	1
18	Composite resins	3
19	Adhesives systems	7
20	Glass ionomer cements	3
21	Dentin sealants	3
22	Laser	21
23	Potassium Citrate	1
24	HEMA	1
25	Others	2

Table 3.1 - Summary of the included studies on systematic review up to 1 day

Author (year)	Study design	Treatment Code	Treatment	Number of teeth	Number of subjects	Mean age/age range and Gender	Mean difference of pain assessment between baseline and follow-up	Percentage of DH reduction between baseline and final follow-up
Ozen *et al.* 2009[36]	Parallel	**1**	Distilled Water (Placebo)	208	52	33.42 26 M /26 W	-2.23	3.6
		2	3% Potassium Nitrate (Ultra EZ)				-10.77	17
		5	Sodium Fluoride (Duraphat)				-9.15	16
		12	Glutaraldehyde (Gluma Desensitizer)				-8.23	15.1
Yilmaz *et al.* 2011[37]	Split-mouth	**1**	NaF Placebo	64	48	41 22 M / 26W	-3.8	5.9
		1	LASER Placebo	64			-2.3	3.7
		5	NaF Varnish	58			-54	79.9
		22	GaAlAs Diode LASER 500mW 810 nm	58			-46.7	74.1
Brahmbhatt *et al.* 2012[20]	Split-mouth	**1**	Iontophoresis Water (placebo) (Desensitron II)	70	25	20-50 NR	NR	29
		5	2% Sodium Fluoride Solution	64			NR	41
		10	Iontophoresis 2% Sodium Fluoride Solution (Desensitron II)	65			NR	89
		12	5% Gluteraldehyde (GLUMA®)	65			NR	80
Vora *et al.* 2012[38]	Split-mouth	**1**	Water (placebo)	150	50	32.4 32 M / 18 W	-33.8	51.7
		9	Oxalic Acid (BisBlock)				-26	41.8
		12	Glutaraldehyde (Gluma Desensitizer PowerGel)				-50	77.4
Bal *et al.* 2015[35]	Split-mouth	**1**	Placebo	22	21	37 5 M / 16 W	-1.09	2.9
		11	8% Arginine Calcium Carbonate Dentifrice (DP) (Colgate Sensitive Pro-Relif)	32			-19.78	36
		22	Low Level Laser 685 nm 25 mW (LLL)	41			-23.41	48.8
		11 + 22	LLL followed by DP	29			-25.28	46
		11 + 22	DP followed by LLL	32			-20.9	34
Orhan *et al.* 2011[39]	Parallel	**1**	Distilled Water (Placebo)	16	16	34.31 8 M/ 8 W	-2.25	3,7
		1	Placebo LASER	16			-0.75	1,1
		12	Glutaraldehyde (Gluma Desensitizer)	16			-26.25	40.4
		22	GaAlAs Diode LASER Low Level 655 nm 25mW	16			-29.5	43.5
Aranha *et al.* 2012[40]	Parallel	**1**	Control (no treatment)	7	28	NR	-19	NC
		22	Er:YAG LASER (0,64W/5.9 J/cm2)	7			-29.4	NC
		22	Er,Cr:YSGG LASER (0.25 W/4.4 J/cm2)	7			-15.7	NC
		22	Er,Cr:YSGG LASER (0.50 W/ 8.9 J/cm2)	7			-18.7	NC
Yilmaz *et al.* 2011[41]	Split-mouth	**1**	Control (no treatment)	174	51	44 22 M / 29 W	-3	4,3
		22	Er,Cr:YSGG LASER 2780 nm 0,25W				-57	79.2

		22	GaAlAs Diode LASER 810 nm				-54	76.1
Yilmaz *et al.* 2011[42]	Split-mouth	**1**	LASER Er, Cr:YSGG without emission (Placebo)	146	42	33.8	-7.6	11
		22	LASER Er, Cr:YSGG 0,25W			18 M / 24 W	-55.5	79.1
Dilsiz *et al.* 2010[43]	NR	**1**	Not Irradiated (control)	96	24	34 11 M / 13 W	-0.8	1
		22	Er:YAG LASER 2,940-nm				-7.9	9.5
		22	Nd:YAG LASER 1064 nm 1W				-33.4	39.9
		22	GaAlAs Diode LASER 808 nm 100mW				-5.4	6.5
Hoang-Dao *et al.* 2009[44]	Split-mouth	**2**	Potassium Nitrate (Isodan)	10	10	33.42 2 M / 8 W	-8	26.7
		5	5% NaF Varnish (Shellac F)	20			-10	25.6
		5	NaF Varnish (Duraphat)	10			-15	46.9
França *et al.* 2015[45]	Parallel	**2**	Potassium nitrate-based toothpaste (Villevie prophylactic pasteb + Sensodyne Pronamelc, potassium nitrate and sodium fluoride- toothpaste)	NR	50	34.18 13 M / 37 W	-6	7.6
		11	8% arginine and calcium carbonate (Colgate Sensitive Pro-Relief Toothpaste) + 8% arginine, calcium carbonate and 1,450 ppm fluoride (Colgate Sensitive Pro-Relief Desensitizing Paste with Pro-Arginine Technology)				-20	25.3
Dilsiz *et al.* 2010[46]	NR	**3**	3.75% Potassium Chloride Dentifrice (Sensodyne F)	26	13	31.2 6 M / 7 W	-5.4	6.7
		3 + 22	Erbium and Diode LASER 100 mW 808 nm + 3.75% Potassium Chloride Dentifrice (Sensodyne F)	26			-8.5	10.5
Osmari *et al.* 2018[47]	Split-mouth	**5**	5% NaF Varnish (Duraphat)	76	19	NR 6 M / 13 W	-26.95	47.1
		9	3% Potassium Oxalate Gel (Oxa-Gel)				-15.32	26.7
		19	Self-Etch Adhesive (Clearfil SE Bond)				-1.42	3
		22	High Intensity Diode LASER 810–830 nm 0.5–4.5 W				-9.95	18
Idon *et al.* 2017[4]	Split-mouth	**1**	Distilled Water (Placebo)	127	68	33.8 36 M /32 W	3	-5.7
		5	5% NaF Varnish (Copal F)	127			-39	69.6
		11	8% Arginine Calcium Carbonate Dentifrice (Pro-Relief)	127			-32	55.2
		12	5% Glutaraldehyde (Gluma Desensitizer)	127			-39	67.2
Soares *et al.* 2016[48]	Split-mouth	**1**	2% Sodium Fluoride Gel (Flugel)	27	23	20-65 3 M / 20 W	-25	NC
		22	GaAlAs LASER, 40 mW	29			-52	NC
		22	Nd:YAG LASER, 1 W	33			-49.4	NC
Ravishankar *et al.* 2018[49]	Parallel	**5**	5% NaF Varnish (Profluorid Varnish)	28	28	18-60 NR	-32	88.9
		19	Admira Protect	28			-25	100
		19	PRG-Barrier Coat	28			-30	100
Pinna *et al.* 2015[50]	Split-mouth	**5**	4 a 6 % NaF Varnish (Flor-Opal® Varnish)	31	46	NR 19 M / 27 W	-20	50
		18	Flow Resin (Vertice Flow)	28			-30	75
		19	Adhesive (Clearfil Protect Bond)	30			-20	50

		21	Sealant (Universal Dentine Sealant)	27			-30	60
Femiano *et al.* 2013[51]	Split-mouth	**5**	2% NaF solution	65	24	38 8 M / 16 W	-33	51.6
		12	Glutaraldehyde (Gluma desensitizer)	67			-50	75.8
		22	Diode LASER 320 nm	69			-52	72.2
		5 + 22	NaF + Diode LASER	61			-57	82.6
Kara *et al.* 2009[52]	Parallel	**5**	NaF Varnish (Bifluorid 12)	NR	20	37 8 M / 12 W	-20.3	28.6
		22	Nd:YAG LASER 1.064 2W	NR			-46.8	66.7
Torres *et al.* 2014[53]	Split-mouth	**5**	6% NaF Varnish (Biflouride 12)	225	40	NR	-10.3	30.6
		11	8% Arginine Calcium Carbonate Dentifrice (DP) (Colgate				-10.3	37.5
		19	Admira Protect				-17.4	50.3
Seong *et al.* 2018[54]	Parallel	**5**	NaF Dentifrice (Crest® Decay Prevention Toothpaste)	NR	19	43.5 1 M / 18 W	-12.2	35.3
		8	8% strontium acetate Dentifrice (Sensodyne® Rapid Relief)	NR			-1.1	2.7
He *et al.* 2011[55]	Parallel	**5**	0,76% sodium monofluorophosphate (Colgate Cavity Protection)	NR	111	44.1 35 M / 76 W	-2.26	2.9
		6	0,454% stannous fluoride (Crest® Pro-Health™ Sensitive Shield)	NR			-11.65	15.1
Mason *et al.* 2010[56]	Parallel	**5**	1450 NaF Dentifrice	NR	79	41.6 12 M / 67 W	-9.3	20
		6	8% Strontium Acetate Dentifrice (Sensodyne Rapid Relief)	NR			-18.1	45
Parkinson *et al.* 2016 (study 1)[57]	Parallel	**5**	0,76% sodium monofluorophosphate (Colgate Cavity Protection)	NR	118	36.3 44 M / 74 W	-7.97	13.2
		6	0.454% w/w stannous fluoride dentifrice (Crest Sensitivity - Treatment and Protection)	NR			-11.29	18.8
Parkinson *et al.* 2016 (study 3)[57]	Parallel	**5**	0,76% sodium monofluorophosphate (Colgate Cavity Protection)	NR	120	29.5 45 M / 75 W	-9.12	15.2
		6	0.454% stannous fluoride dentifrice	NR			-4.05	7.6
He *et al.* 2011[58]	Parallel	**6**	Stannous-containing 1450 ppm sodium fluoride dentifrice (Pro-Expert)	NR	81	43.25 6 M / 75 W	-16.2	23.2
		11	8% arginine, calcium carbonate, and 1450 ppm fluoride (Colgate Pro-Relief)	NR			-0.6	0.8
West *et al.* 2013[59]	Parallel	**8**	8% Strontium Acetate Dentifrice (Sensodyne Rapid Relief)	NR	80	NR 25 M / 55 W	-9.12	NC
		11	8% Arginine Calcium Carbonate Dentifrice (Colgate Sensitive Pro-Relief)	NR			-8.7	NC
Erdemir *et al.* 2010[60]	Split-mouth	**9**	Oxalic Acid Gel 2% (Pain-Free)	44	11	47 4 M /7 W	-14.3	42.8
		9	Oxalic Acid Gel (BisBlock)	43			-27.4	51.0
		18	Resine (Seal and Protect)	44			-32.8	63.8
Talesara *et al.* 2014[61]	Split-mouth	**9**	Potassium Binoxalate Gel (D/Sens Crystal)	40	20	25 - 55 10 M / 10 W	-62	79.5
		22	Nd:YAG LASER, 1W	40			-60	81.1

Patil *et al.* 2015[62]	Parallel	**12**	Glutaraldehyde (Gluma Desensitizer)	18	20	18 - 35 8 M / 12 W	-46	63
		19	Universal Adhesive (Single Bond Universal)	18			-47	63.5
		12 + 19	Glutaraldehyde with Adhesive (Gluma Comfort Bond + Gluma Desensitizer)	18			-43	58.9
Lopes *et al.* 2017[63]	Split-mouth	**12**	Glutaraldehyde (Gluma Desensitizer)	13	32	22 - 53 NR	-35	74.5
		22	LASER Low Power Low Dose (LPLD) 810 nm 30 mW	13			-12	51.1
		22	LASER Low Power High Dose (LPHD) 810nm 100 mW	13			-13.5	36.5
		22	Nd:YAG LASER 1064 nm 1 W	13			-26	56.5
		22 + 22	LPLD + Nd:YAG LASER 1064 nm	13			-19.5	45.9
		22 + 22	LPHD + Nd:YAG LASER 1064 nm	13			-24.5	40.2
		12 + 22	LPLD + Glutaraldehyde (Gluma Desensitizer)	13			-40	65.6
		12 + 22	LPHD + Glutaraldehyde (Gluma Desensitizer)	13			-15	23.1
		22 + 12	Nd:YAG LASER + Glutaraldehyde (Gluma Desensitizer)	13			-42	71.2
Lopes *et al.* 2015[64]	Split-mouth	**12**	Glutaraldehyde (Gluma Desensitizer)	11	27	22 - 53 NR	-20.21	43
		22	Low Power Laser Low Dose 30mW 810 nm (LPLLD)	11			-10.34	44
		22	Low Level Laser High Dose 100mW 810 nm (LPLHD)	11			-10.73	29
		22 + 12	LPLLD + Glutaraldehyde (Gluma Desensitizer)	11			-29.28	48
		22 + 12	LPLHD + Glutaraldehyde (Gluma Desensitizer)	11			-20.8	32
Sethna *et al.* 2011[65]	Split-mouth	**12**	5% Glutaraldehyde (Gluma Desensitizer)	NR	250	20 - 55 140 M / 160	-28.9	41.9
		13	1% Chlorhexidine (Cervitec)	NR			-41.7	58.7
Canali *et al.* 2017[66]	Split-mouth	**19**	Self-Etch Adhesive (Clearfil SE Protect)	179	30	32,5 NR	-45	90
		19	Total Etch Adhesive with Glutaraldehyde (Gluma 2 Bond)				-46	83.6
		20	Resin-Modified GIC (ClinproTM XT)				-52	88.1
Madruga *et al.* 2017[67]	Split-mouth	**20**	Resin-Modified GIC (ClinproTM XT)	70	20	42.7 3 M / 17 W	-37	72.5
		20	Convencional GIC (Vidrion R)	82			-42	70
Ding *et al.* 2014[27]	Split-mouth	**1**	Warm water (placebo)	119	31	46.9 13 M / 18 W	NS VNR	
		12	Gulma Dentin Desensitizer				SS VNR	
		20	Clinpro XT Varnish				SS VNR	
Mehta *et al.* 2015[31]	Split-mouth	**1**	Distilled Water (Placebo)	NR	35	33.3 10 M / 25 W	SS VNR	
		15	Teethmate AP	NR			SS VNR	
Mehta *et al.* 2014[30]	Parallel	**12**	Glutaraldehyde (Gluma Desensitizer Power Gel)	NR	49	NR 16 M / 34 W	SS VNR	
		15	Teethmate Desensitizer	NR			SS VNR	
		21	NanoSeal	NR			SS VNR	
		21	MS Coat One F	NR			SS VNR	
Lopes *et al.* 2013[29]	Split-mouth	**12**	Glutaraldehyde (Gluma Desensitizer)	11	24	NR NR	NS VNR	
		22	Nd:YAG Laser 1.5W, 10Hz, 100mJ	11			SS VNR	
		12 + 22	Nd:YAG Laser + Gluma Desensitizer	11			SS VNR	

M: men; **W:** women; **NR:** not reported; **NC:** not calculated; **CNR:** composition not reported; **SS:** statistically significant; **NS:** not statistically significant; **VNR:** values not reported; ***** medium of the 4 quadrants values

Table 3.2 - Summary of the included studies on systematic review from 2 to 7 days

Author (year)	Study design	Treatment Code	Treatment	Number of teeth	Number of subjects	Mean age/age range and Gender	Mean difference of pain assessment between baseline and follow-up	Percentage of DH reduction between baseline and final follow-up
Ozen *et al.* 2009[36]	Parallel	**1**	Distilled Water (Placebo)	208	52	17-51 26 M / 26 W	-1.62	2.6
		2	3% Potassium Nitrate (Ultra EZ)				-57.38	90.4
		5	Sodium Fluoride (Duraphat)				-51.53	90.2
		12	Glutaraldehyde (Gluma Desensitizer)				-48.07	88.4
Yilmaz *et al.* 2011[37]	Split-mouth	**1**	NaF Placebo	64	48	41 22 M / 26W	-3.2	5.0
		1	LASER Placebo	64			-1.5	2.4
		5	NaF Varnish	58			-54.8	81.1
		22	GaAlAs Diode LASER 500mW 810 nm	58			-47.9	76
Vora *et al.* 2012[38]	Split-mouth	**1**	Water (placebo)	150	50	32.4 32 M / 18 W	-33.8	51.7
		9	Oxalic Acid (BisBlock)				-21.6	34.7
		12	Glutaraldehyde (Gluma Desensitizer PowerGel)				-48.1	74.5
Orhan *et al.* 2011[39]	Parallel	**1**	Distilled Water (Placebo)	16	16	34.31 8 M / 8 W	-2.25	3,7
		1	Placebo LASER	16			0	0
		12	Glutaraldehyde (Gluma Desensitizer)	16			-55.25	85
		22	GaAlAs Diode LASER Low Level 655 nm 25mW	16			-59	87.1
Aranha *et al.* 2012[40]	Parallel	**1**	Control (no treatment)	7	28	NR	-12.3	NC
		22	Er:YAG LASER (0,64W/5.9 J/cm2)	7			-27	NC
		22	Er,Cr:YSGG LASER (0.25 W/4.4 J/cm2)	7			-3.4	NC
		22	Er,Cr:YSGG LASER (0.50 W/ 8.9 J/cm2)	7			-19.3	NC
Yilmaz *et al.* 2011[41]	Split-mouth	**1**	Control (no treatment)	174	51	44 22 M / 29 W	-4	5.8
		22	Er,Cr:YSGG LASER 2780 nm 0,25W				-60	83.3
		22	GaAlAs Diode LASER 810 nm				-55	77.5
Yilmaz *et al.* 2011[42]	Split-mouth	**1**	LASER Er, Cr:YSGG without emission (Placebo)	146	42	33.8 18 M / 24 W	-7.7	11.2
		22	LASER Er, Cr:YSGG 0,25W				-54.3	77.4
Idon *et al.* 2017[4]	Split-mouth	**1**	Distilled Water (Placebo)	127	68	33.8 36 M /32 W	2	-3.8
		5	5% NaF Varnish (Copal F)	127			-40	71.4
		11	8% Arginine Calcium Carbonate Dentifrice (Pro-Relief)	127			-32	55.2
		12	5% Glutaraldehyde (Gluma Desensitizer)	127			-42	72.4
Soares *et al.* 2016[48]	Split-mouth	**5**	2% Sodium Fluoride Gel (Flugel)	27	23	20-65 3 M / 20W	-30	NC
		22	GaAlAs LASER, 40 mW	29			-65.3	NC
		22	Nd:YAG LASER, 1 W	33			-65.9	NC
Ravishankar *et al.*	Parallel	**5**	5% NaF Varnish (Profluorid Varnish)	28	28	18-60	-16	44.4

2018[49]		**19**	Admira Protect	28		NR	-25	100
		19	PRG-Barrier Coat	28			-27	90
Pinna *et al.* 2015[50]	Split-mouth	**5**	4 a 6 % NaF Varnish (Flor-Opal® Varnish)	31	46	NR 19 M / 27 W	-20	50
		18	Flow Resin (Vertice Flow)	28			-30	75
		19	Adhesive (Clearfil Protect Bond)	30			-20	50
		21	Sealant (Universal Dentine Sealant)	27			-30	60
Kara *et al.* 2009[52]	Parallel	**5**	NaF Varnish (Bifluorid 12)	NR	20	37 8 M / 12 W	-30.1	42.5
		22	Nd:YAG LASER 1.064 2W	NR			-48.1	68.5
Torres *et al.* 2014[53]	Split-mouth	**5**	6% NaF Varnish (Biflouride 12)	225	40	NR	-9.3	27.6
		11	8% Arginine Calcium Carbonate Dentifrice (Colgate Sensitive Pro-Relief)				-10.7	38.9
		19	Admira Protect				-16	46.2
He *et al.* 2011[55]	Parallel	**5**	0,76% sodium monofluorophosphate (Colgate Cavity Protection)	NR	111	44.1 35 M / 76 W	-3.23	4.1
		6	0,454% stannous fluoride (Crest® Pro-Health™ Sensitive Shield)	NR			-27.7	36
Mason *et al.* 2010[56]	Parallel	**5**	1450 NaF Dentifrice	NR	79	41.6 12 M / 67 W	-14	30
		6	8% Strontium Acetate Dentifrice (Sensodyne Rapid Relief)	NR			-23.9	59
Parkinson *et al.* 2016 (study 1)[57]	Parallel	**5**	0,76% sodium monofluorophosphate (Colgate Cavity Protection)	NR	118	36.3 44 M / 74 W	-13.48	22.3
		6	0.454% wfw stannous fluoride dentifrice (Crest Sensitivity - Treatment and Protection)	NR			-17.16	28.5
Parkinson *et al.* 2016 (study 3)[57]	Parallel	**5**	0,76% sodium monofluorophosphate (Colgate Cavity Protection)	NR	120	29.5 45 M / 75 W	-12.47	20.7
		6	0.454% stannous fluoride dentifrice	NR			-10.82	20.2
He *et al.* 2011[58]	Parallel	**6**	Stannous-containing 1450 ppm sodium fluoride dentifrice (Pro-Expert)	NR	81	43.25 6 M / 75 W	-53.8	77.1
		11	8% arginine, calcium carbonate, and 1450 ppm fluoride (Colgate Pro-Relief)	NR			-6.4	9
West *et al.* 2013[59]	Parallel	**8**	8% Strontium Acetate Dentifrice (Sensodyne Rapid Relief)	NR	80	NR 25 M / 55 W	-12.05	NC
		11	8% Arginine Calcium Carbonate Dentifrice (Colgate Sensitive Pro-Relief)	NR			-16.86	NC
Erdemir *et al.* 2010[60]	Split-mouth	**9**	Oxalic Acid Gel 2% (Pain-Free)	44	11	47 4 M /7 W	-12.7	38
		9	Oxalic Acid Gel (BisBlock)	43			-19.5	36.3
		18	Resin (Seal and Protect)	44			-28.2	54.9
Lopes *et al.* 2015[64]	Split-mouth	**12**	Glutaraldehyde (Gluma Desensitizer)	11	27	22 - 53 NR	-27.73	59
		22	Low Power Laser Low Dose 30mW 810 nm (LPLLD)	11			-14.1	60
		22	Low Level Laser High Dose 100mW 810 nm (LPLHD)	11			-32.19	87
		22 + 12	LPLLD + Glutaraldehyde (Gluma Desensitizer)	11			-48.19	79
		22 + 12	LPLHD + Glutaraldehyde (Gluma Desensitizer)	11			-48.75	75

Madruga *et al.* 2017[67]	Split-mouth	**20**	Resin-Modified GIC (ClinproTM XT)	70	20	42.7	-43	84.3
		20	Conventional GIC (Vidrion R)	82		3 M / 17 W	-50	83.3
Antoniazzi *et al.* 2014[68]	Parallel	**1**	Placebo Gel	36	107	42.94 55 M / 71 W	-2.7	3.7
		5	2% Sodium Fluoride Gel (Flugel)	37			-16.8	24.1
		5 + 9 + 14	5% NaF, 5% Potassium Oxalate and 10% Strontium Chloride Gel	34			-36.1	47.8
Tirapelli *et al.* 2011[69]	Parallel	**2**	5% Potassium Nitrate Dentifrice (Sensodyne)	52	120	NR	-22	33.8
		15	Sensi Kill®	62			-21	33.9
		15	Bioactive Glass Gel (Biosilicate® gel)	59			-26	37.7
		15	Bioactive Glass powder (Biosilicate® powder)	59			-40	59.7
Jalali *et el.* 2010[70]	Parallel	**4**	Varnish Containing Potassium Fluoride (VivaSens)	111	27	38	-24.75*	72.3*
		21	Resin-based Sealing Material (Seal and Protect)	103		NR	-22*	76.5*
Dantas *et al.* 2016[71]	Split-mouth	**5**	5% NaF varnish (Fluorniz®)	40	NR	NR	-14	32
		22	Low-level laser radiation 4J/cm2	46		NR	-8.9	21.3
Hall *et al.* 2017[72]	Parallel	**5**	Dentifrice (Negative Control) (Colgate Triple Protection)	45	133	37.4 27 M / 106 W	-5.15	7.7
		11	8% Arginine Calcium Carbonate Dentifrice (Sensitive Pro-Relief)	43			-14.61	23.1
		15	5% Calcium Sodium Phosphosilicate (CSPS) Dentifrice (Sensodyne ® Repair & Protect)	45			-15.32	22.3
Guentsch *et al.* 2012[73]	Parallel	**12**	Glutaraldehyde (control) (Gluma® Desensitizer)	53	40	34.63	-15	21.4
		25	Biomimetic mineralization system (BIMIN)	58		11 M / 29 W	-17	24.3
Ding *et al.* 2014[27]	Split-mouth	**1**	Warm water (placebo)	119	31	46.9 13 M / 18 W		NS VNR
		12	Gulma Dentin Desensitizer					SS VNR
		20	Clinpro XT Varnish					SS VNR
Han *et al.* 2017[74]	Parallel	**9**	BisBlock	43	64	46.4 27 M / 37 W	-14.5	23.1
		9	SuperSeal	45			-26.4	38.1
		12 + 24	Gluma Desensitizer	45			-17.9	28.5
		15	DeSen	30			-13.4	21.4
		5 + 24	Hurriseal Dentin Desensitizer	52			-21.5	33.7
Raichur *et al.* 2012[32]	Parallel	**2**	5 % Potassium Nitrate Gel	NR	54	25-45 30 M / 24 W		SS VNR
		6	0,4 % Stannous fluoride gel	NR				SS VNR
		22	LASER GaAlAs 940nm DL	NR				SS VNR
Mehta *et al.* 2015[31]	Split-mouth	**1**	Distilled Water (Placebo)	NR	35	33.3 10 M / 25 W		SS VNR
		15	Teethmate AP	NR				SS VNR
Mehta *et al.* 2014[30]	Parallel	**12**	Glutaraldehyde (Gluma Desensitizer Power Gel)	NR	49	NR 16 M / 34 W		SS VNR
		15	Teethmate Desensitizer	NR				SS VNR
		21	NanoSeal	NR				SS VNR
		21	MS Coat One F	NR				SS VNR
Lopes *et al.*	Split-mouth	**12**	Glutaraldehyde (Gluma Desensitizer)	11	24	NR		SS VNR

2013[29]	**22**	Nd:YAG Laser 1.5W, 10Hz, 100mJ	11	NR	SS VNR
	12 + 22	Nd:YAG Laser + Gluma Desensitizer	11		SS VNR

M: men; **W:** women; **NR:** not reported; **NC:** not calculated; **CNR:** composition not reported; **SS:** statistically significant; **NS:** not statistically significant; **VNR:** values not reported; ***** medium of the 4 quadrants values

Table 3.3 - Summary of the included studies on systematic review from 8 to 15 days

Author (year)	Study design	Treatment Code	Treatment	Number of teeth	Number of subjects	Mean age/age range and Gender	Mean difference of pain assessment between baseline and follow-up	Percentage of DH reduction between baseline and final follow-up
Brahmbhatt *et al.* 2012[20]	Split-mouth	**1**	Iontophoresis Water (Placebo) (Desensitron II)	70	25	20-50 NR	NR	19
		5	2% Sodium Fluoride Solution	64			NR	55
		10	Iontophoresis 2% Sodium Fluoride Solution (Desensitron II)	65			NR	96
		12	5% Glutaraldehyde (GLUMA®)	65			NR	93
Bal *et al.* 2015[35]	Split-mouth	**1**	Placebo	22	21	37 5 M / 16 W	3.23	-8.5
		11	8% Arginine Calcium Carbonate Dentifrice (Colgate Sensitive Pro-Relief)	32			-28.95	52.7
		22	Low Level Laser 685 nm 25 mW (LLL)	41			-27.25	56.8
		11 + 22	LLL followed by DP	29			-25.35	46.2
		11 + 22	DP followed by LLL	32			-24.37	40.6
Dilsiz *et al.* 2010[43]	NR	**1**	Not Irradiated (control)	96	24	34 11 M / 13 W	-0.8	1
		22	Er:YAG LASER 2,940-nm				-52.9	63.5
		22	Nd:YAG LASER 1064 nm 1W				-72.5	86.5
		22	GaAlAs Diode LASER 808 nm 100mW				-38.3	46.2
França *et al.* 2015[45]	Parallel	**2**	Potassium nitrate-based toothpaste (Villevie prophylactic paste + Sensodyne Pronamelc, potassium nitrate and sodium fluoride-toothpaste)	NR	50	34.18 13 M / 37 W	-20	25.3
		11	8% arginine and calcium carbonate (Colgate Sensitive Pro-Relief Toothpaste) + 8% arginine, calcium carbonate and 1,450 ppm fluoride (Colgate Sensitive Pro-Relief Desensitizing Paste with Pro-Arginine Technology)				-32	40.5
Dilsiz *et al.* 2010[46]	NR	**3**	3.75% Potassium Chloride Dentifrice (Sensodyne F)	26	13	31.2 6 M / 7 W	-27.7	34.5
		3 + 22	Erbium and Diode LASER 100 mW 808 nm + 3.75% Potassium Chloride Dentifrice (Sensodyne F)	26			-59.6	73.8
Osmari *et al.* 2018[47]	Split-mouth	**5**	5% NaF Varnish (Duraphat)	76	19	NR 6 M / 13 W	-22.9	40.1
		9	3% Potassium Oxalate Gel (Oxa-Gel)				-23.95	41.8
		19	Self-Etch Adhesive (Clearfil SE Bond)				-12.1	25.2
		22	High Intensity Diode LASER 810–830 nm 0.5–4.5 W				-19.89	36
Idon *et al.* 2017[4]	Split-mouth	**1**	Distilled Water (Placebo)	127	68	33.8 36 M /32 W	1	-1.9
		5	5% NaF Varnish (Copal F)	127			-47	83.9
		11	8% Arginine Calcium Carbonate Dentifrice (Pro-Relief)	127			-45	77.6
		12	5% Glutaraldehyde (Gluma Desensitizer)	127			-49	84.5

Kara *et al.* 2009[52]	Parallel	**5**	NaF Varnish (Bifluorid 12)	NR	20	37	-50	70.5
		22	Nd:YAG LASER 1.064 2W	NR		8 M / 12 W	-47.7	67.9
Torres *et al.* 2014[53]	Split-mouth	**5**	6% NaF Varnish (Biflouride 12)	225	40	NR	-14.7	43.6
		11	8% Arginine Calcium Carbonate Dentifrice (Colgate Sensitive Pro-Relief)			NR	-11.7	42.5
		19	Admira Protect				-15.4	44.5
He *et al.* 2011[55]	Parallel	**5**	0,76% sodium monofluorophosphate (Colgate Cavity Protection)	NR	111	44.1	-8.01	10.2
		6	0,454% stannous fluoride (Crest® Pro-Health™ Sensitive Shield)	NR		35 M / 76 W	-53.31	69.3
Parkinson *et al.* 2016 (study 1)[57]	Parallel	**5**	0,76% sodium monofluorophosphate (Colgate Cavity Protection)	NR	118	36.3	-23.28	38.5
		6	0.454% w/w stannous fluoride dentifrice (Crest Sensitivity - Treatment and Protection)	NR		44 M / 74 W	-30.30	50.4
Parkinson *et al.* 2016 (study 3)[57]	Parallel	**5**	0,76% sodium monofluorophosphate (Colgate Cavity Protection)	NR	120	29.5	-19.77	32.9
		6	0.454% stannous fluoride dentifrice	NR		45 M / 75 W	-23.74	44.3
Erdemir *et al.* 2010[60]	Split-mouth	**9**	Oxalic Acid Gel 2% (Pain-Free)	44	11	47	-19.1	57.2
		9	Oxalic Acid Gel (BisBlock)	43		4 M /7 W	-24.4	45.4
		18	Resin (Seal and Protect)	44			-33	64.2
Madruga *et al.* 2017[67]	Split-mouth	**20**	Resin-Modified GIC (ClinproTM XT)	70	20	42.7	-44	86.3
		20	Conventional GIC (Vidrion R)	82		3 M / 17 W	-50	83.3
Antoniazzi *et al.* 2014[68]	Parallel	**1**	Placebo Gel	36	107	42.94	-12.2	16.9
		5	2% Sodium Fluoride Gel (Flugel)	37			-26.8	38.5
		5 + 9 + 14	5% NaF, 5% Potassium Oxalate and 10% Strontium Chloride Gel	34		55 M / 71 W	-45.6	60.3
Tirapelli *et al.* 2011[69]	Parallel	**2**	5% Potassium Nitrate Dentifrice (Sensodyne)	52	120	NR	-29	44.6
		15	Sensi Kill®	62			-31	50
		15	Bioactive Glass Gel (Biosilicate® gel)	59		NR	-32	46.4
		15	Bioactive Glass powder (Biosilicate® powder)	59			-44	65.7
Hall *et al.* 2017[72]	Parallel	**5**	Dentifrice (Colgate Triple Protection)	45	133	37.4 27 M / 106 W	-10.92	16.4
		11	8% Arginine Calcium Carbonate Dentifrice (Sensitive Pro-Relief)	43			-18.77	29.7
		15	5% Calcium Sodium Phosphosilicate (CSPS) Dentifrice (Sensodyne ® Repair & Protect)	45			-21.17	30.8
Pradeep *et al.* 2012[75]	Parallel	**1**	Placebo Dentifrice	NR	149	39.85	-10.8	20.3
		2	5% Potassium Nitrate Dentifrice (SHY)	NR			-12.3	22.4
		7	3.85% Amine Fluoride Dentifrice (AMFLOR)	NR		72 M / 77 W	-13.2	24.2
		15	5% Calcium Sodium Phosphosilicate Dentifrice (SHY-NM)	NR			-17.7	31.9
Pradeep *et al.*	Parallel	**1**	Placebo Dentifrice	NR	110	39.4	-12	18.8

2010[75]		**2**	5% Potassium Nitrate Dentifrice (SHY)	NR		58 M / 52 W	-9.1	13.9
		15	5% Calcium Sodium Phosphosilicate Dentifrice (SHY-NH)	NR			-24.6	34.3
Vano *et al.* 2014[76]	Parallel	**1**	Water (Placebo)	NR	105	42 48 M / 57 W	-1.24	2.2
		5	Fluoride Dentifrice (Colgate Cavity Protection Regular)	NR			-3.52	6.4
		15	15% Nano Hydroxyapatite Dentifrice (PrevDent)	NR			-16.8	29.9
Vano *et al.* 2018[77]	Parallel	**1**	Glycerin (placebo)	NR	105	42 40 M / 65 W	1.86	-3.3
		5	NaF Dentifrice (Colgate Cavity Gel) (Positive Control)	NR			-3.87	6.8
		15	2% Nano-hydroxyapatite Dentifrice (Cavex Bite&White)	NR			-16.37	27.5
Du Min *et al.* 2008[78]	Parallel	**1**	Negative Control Dentifrice Without NovaMin	NR	71	44.1 34 M / 41 W	NR	15.2
		14	Strontium Chloride Dentifrice (Leng Suan Ling Toothpaste)	NR			NR	14.7
		15	5% NovaMin Dentifrice	NR			NR	17.6
Litkowski *et al.* 2010[34]	Parallel	**1**	Placebo Dentifrice	NR	66	38.8 12 M / 54 W	-2.6	5
		15	2.5% Novamin Dentifrice	NR			-5.1	9
		15	7.5% Novamin Dentifrice	NR			-13.9	26
Majji *et al.* 2016[79]	Parallel	**2**	5% Potassium Nitrate Dentifrice (RA Thermoseal)	NR	240	20 - 60 93 M / 67 W	-8.5	11.8
		14	3-10% Strontium Chloride Dentifrice (Thermoseal®)	NR			-19.2	26.3
		15	5% Calcium Sodium Phosphosilicate (Novamin) Dentifrice (Vantej)	NR			-30.2	41.9
		16	Herbal Dentifrice (Wheezal dental cream)	NR			-8.5	12
Katanec *et al.* 2016[80]	Parallel	**2**	5% Potassium Nitrate Dentifrice (ProSensitive)	NR	74	NR	-11.8	17.9
		5	Dentifrice without Potassium Nitrate (ProSensitive)	NR		NR	-11.9	16.8
Sharma *et al.* 2013[81]	Parallel	**2**	5% KNO3 Dentifrice (Sensodyne® Original)	NR	226	36.3 73 M / 153 W	-12.2	23.9
		5	NaF Dentifrice (Crest Cavity Protection Regular)	NR			-7.5	14.6
		2 + 5	Potassium Oxalate Mouthrinse (Listerine Advanced Defense Sensitive) + NaF Dentifrice (Crest Cavity Protection Regular)	NR			-10.7	21.2
Salian *et al.* 2010[82]	Parallel	**1**	Control Dentifrice (CNR)	NR	30	20 - 50	0.3	-0.5
		2	5% Potassium Nitrate Dentifrice	NR			-0.5	0.9
		15	5% Calcium Sodium Phosphosilicate Dentifrice (Novamin)	NR			-19.6	34
Sharma *et al.* 2010[83]	Parallel	**2**	5% Potassium Nitrate Dentifrice (Sensodent K)	NR	120	31.7 60 M / 60 W	-20.5	35
		6	0.4% Stannous Fluoride Dentifrice	NR			-17.3	29.7
		15	7.5% Calcium Sodium Phosphosilicate (Novamin) Dentifrice	NR			-25.8	45
Gibson *et al.* 2013[84]	Parallel	**5**	Non-desensitizing Toothpaste (Colgate Cavity Protection Regular)	NR	72		-7.26	12.9
		21	Desensitizing Agent (Seal and Protect, Dentsply)	NR		48.21	-50.15	81.8
		23	Desensitizing Toothpaste (Colgate Sensitive Fresh Stripe)	NR		19 M / 53 W	-15.67	27.8
Hughes *et al.*	Parallel	**8**	8% Strontium Acetate Dentifrice (Sensodyne Rapid Relief)	NR	78	26.45	-9.2	21.3

2010[85]		**11**	8% Arginine Calcium Carbonate Dentifrice (Colgate Sensitive Pro-Relief)	NR		37 M / 41 W	-7.6	17.5
Ko *et al.* 2014[86]	Parallel	**22**	LASER Toothbrush (635 nm e 6 mW)	NR	86	40.65	-19	32.8
		25	LED Toothbrush (635 nm e12.9 µW)	NR		29 M / 57 W	-12	18.8
Zang et al. 2016[33]	Parallel	**5**	Dentifrice containing 1400ppm fluoride as AMFP (Chinese Colgate Triple Protection)	NR	133		SS VNR	
		15	2,5 % CSPS (4µm) and 1450 ppm fluoride as NaF	NR		40.76	SS VNR	
		15	5 % CSPS (4µm) and 1450 ppm fluoride as NaF	NR		17 M /	SS VNR	
		15	5 % CSPS (14µm) and 1450 ppm fluoride as NaF (Novamin)	NR		117 W	SS VNR	
		15	5 % CSPS (14µm) and 1450 ppm fluoride as NaF (UK Sensodyne Repair and Protect)	NR			SS VNR	
Konekeri *et al.* 2015[28]	Parallel	**2**	Potassium nitrate dentifrice	NR	48	18 - 67	NS VNR	
		25	10 % Casein Phosphopeptide-Amorphous calcium phosphate	NR		NR	SS VNR	

M: men; **W:** women; **NR:** not reported; **NC:** not calculated; **CNR:** composition not reported; **SS:** statistically significant; **NS:** not statistically significant; **VNR:** values not reported; ***** medium of the 4 quadrants values

Table 3.4 - Summary of the included studies on systematic review from 15 to 30 days

Author (year)	Study design	Treatment Code	Treatment	Number of teeth	Number of subjects	Mean age/age range and Gender	Mean difference of pain assessment between baseline and follow-up	Percentage of DH reduction between baseline and final follow-up
Yilmaz *et al.* 2011[37]	Split-mouth	**1**	NaF Placebo	64	48	41 22 M / 26W	-2.4	3.7
		1	LASER Placebo	64			-2.4	4.0
		5	NaF Varnish	58			-53.5	79.1
		22	GaAlAs Diode LASER 500mW 810 nm	58			-49.8	79
Brahmbhatt *et al.* 2012[20]	Split-mouth	**1**	Iontophoresis Water (placebo) (Desensitron II)	70	25	20-50 NR	NR	11
		5	2% Sodium Fluoride Solution	64			NR	34
		10	Iontophoresis 2% Sodium Fluoride Solution (Desensitron II)	65			NR	85
		12	5% Glutaraldehyde (GLUMA®)	65			NR	75
Vora *et al.* 2012[38]	Split-mouth	**1**	Water (placebo)	150	50	32.4 32 M / 18 W	-32.6	49.8
		9	Oxalic Acid (BisBlock)				-19.4	31.2
		12	Glutaraldehyde (Gluma Desensitizer PowerGel)				-48.2	74.6
Bal *et al.* 2015[35]	Split-mouth	**1**	Placebo	22	21	37 5 M / 16 W	3.09	-8.2
		11	8% Arginine Calcium Carbonate Dentifrice (Colgate Sensitive Pro-Relief)	32			-34.2	62.3
		22	Low Level Laser 685 nm 25 mW (LLL)	41			-33.9	70.6
		11 + 22	LLL followed by DP	29			-26.19	48.8
		11 + 22	DP followed by LLL	32			-37.06	61.7
Aranha *et al.* 2012[40]	Parallel	**1**	Control (no treatment)	7	28	NR	-24.6	NC
		22	Er:YAG LASER (0,64W/5.9 J/cm2)	7			-31.6	NC
		22	Er,Cr:YSGG LASER (0.25 W/4.4 J/cm2)	7			-22.6	NC
		22	Er,Cr:YSGG LASER (0.50 W/ 8.9 J/cm2)	7			-16.7	NC
Yilmaz *et al.* 2011[41]	Split-mouth	**1**	Control (no treatment)	174	51	44 22 M / 29 W	-3	4.3
		22	Er,Cr:YSGG LASER 2780 nm 0,25W				-61	84.7
		22	GaAlAs Diode LASER 810 nm				-59	83.1
Yilmaz *et al.* 2011[42]	Split-mouth	**1**	LASER Er, Cr:YSGG without emission (Placebo)	146	42	33.8 18 M / 24 W	-7.5	10.9
		22	LASER Er, Cr:YSGG 0,25W				-57	81.2
Dilsiz *et al.* 2010[43]	NR	**1**	Not Irradiated (control)	96	24	34 11 M / 13 W	0	0
		22	Er:YAG LASER 2,940-nm				-52.9	63.5
		22	Nd:YAG LASER 1064 nm 1W				-73	87.1
		22	GaAlAs Diode LASER 808 nm 100mW				-40.8	49.2

França *et al.* 2015[45]	Parallel	**2**	Potassium nitrate-based toothpaste (Villevie prophylactic paste + Sensodyne Pronamelc, potassium nitrate and sodium fluoride- toothpaste)	NR	50	34.18 13 M / 37 W	-32	40.5
		11	8% arginine and calcium carbonate (Colgate Sensitive Pro-Relief Toothpaste) + 8% arginine, calcium carbonate and 1,450 ppm fluoride (Colgate Sensitive Pro-Relief Desensitizing Paste with Pro-Arginine Technology)				-43	54.4
Dilsiz *et al.* 2010[46]	NR	**3**	3.75% Potassium Chloride Dentifrice (Sensodyne F)	26	13	31.2 6 M / 7 W	-29.2	36.3
		3 + 22	Erbium and Diode LASER 100 mW 808 nm + 3.75% Potassium Chloride Dentifrice (Sensodyne F)	26			-59.6	73.8
Osmari *et al.* 2018[47]	Split-mouth	**5**	5% NaF Varnish (Duraphat)	76	19	NR 6 M / 13 W	-31.89	55.8
		9	3% Potassium Oxalate Gel (Oxa-Gel)				-25.16	43.9
		19	Self-Etch Adhesive (Clearfil SE Bond)				-18.05	37.6
		22	High Intensity Diode LASER 810–830 nm 0.5–4.5 W				-19.84	35.9
Idon *et al.* 2017[4]	Split-mouth	**1**	Distilled Water (Placebo)	127	68	33.8 36 M /32 W	0	0
		5	5% NaF Varnish (Copal F)	127			-50	89.3
		11	8% Arginine Calcium Carbonate Dentifrice (Pro-Relief)	127			-49	84.5
		12	5% Glutaraldehyde (Gluma Desensitizer)	127			-54	93.1
Ravishankar *et al.* 2018[49]	Parallel	**5**	5% NaF Varnish (Profluorid Varnish)	28	28	18-60 NR	-12	33.3
		19	Admira Protect	28			-14	56
		19	PRG-Barrier Coat	28			-13	43.3
Pinna *et al.* 2015[50]	Split-mouth	**5**	4 a 6 % NaF Varnish (Flor-Opal® Varnish)	31	46	NR 19 M / 27 W	-20	50
		18	Flow Resin (Vertice Flow)	28			-25	62.5
		19	Adhesive (Clearfil Protect Bond)	30			-20	50
		21	Sealant (Universal Dentine Sealant)	27			-30	60
Femiano *et al.* 2013[51]	Split-mouth	**5**	2% NaF solution	65	24	38 8 M / 16 W	-19	29.7
		12	Glutaraldehyde (Gluma desensitizer)	67			-37	56.1
		22	Diode LASER 320 nm	69			-45	62.5
		5 + 22	NaF + Diode LASER	61			-48	69.6
Kara *et al.* 2009[52]	Parallel	**5**	NaF Varnish (Bifluorid 12)	NR	20	37 8 M / 12 W	-50.5	71.2
		22	Nd:YAG LASER 1.064 2W	NR			-46.2	65.8
Torres *et al.* 2014[53]	Split-mouth	**5**	6% NaF Varnish (Biflouride 12)	225	40	NR NR	-15.9	47.2
		11	8% Arginine Calcium Carbonate Dentifrice (Colgate Sensitive Pro-Relief)				-9.5	34.5
		19	Admira Protect				-15.6	45.1
Seong *et al.* 2018[54]	Parallel	**5**	NaF Dentifrice (Crest® Decay Prevention Toothpaste)	NR	19	43.5 1 M / 18 W	-24.9	72
		8	8% strontium acetate Dentifrice (Sensodyne® Rapid Relief)	NR			-16.5	40.6

Erdemir *et al.* 2010[60]	Split-mouth	**9**	Oxalic Acid Gel 2% (Pain-Free)	44	11	47 4 M /7 W	-21.6	64.7
		9	Oxalic Acid Gel (BisBlock)	43			-33.7	62.8
		18	Resin (Seal and Protect)	44			-43.4	84.4
Patil *et al.* 2015[62]	Parallel	**12**	Glutaraldehyde (Gluma Desensitizer)	18	20	18 - 35 8 M / 12 W	-63	86.3
		19	Universal Adhesive (Single Bond Universal)	18			-52	70.3
		12 + 19	Glutaraldehyde with Adhesive (Gluma Comfort Bond + Gluma Desensitizer)	18			-62	84.9
Lopes *et al.* 2015[64]	Split-mouth	**12**	Glutaraldehyde (Gluma Desensitizer)	11	27	22 - 53 NR	-39.48	84
		22	Low Power Laser Low Dose 30mW 810 nm (LPLLD)	11			-13.16	56
		22	Low Level Laser High Dose 100mW 810 nm (LPLHD)	11			-32.19	87
		22 + 12	LPLLD + Glutaraldehyde (Gluma Desensitizer)	11			-53.68	88
		22 + 12	LPLHD + Glutaraldehyde (Gluma Desensitizer)	11			-52.65	81
Sethna *et al.* 2011[65]	Split-mouth	**12**	5% Glutaraldehyde (Gluma Desensitizer)	NR	250	20 - 55	-33.8	49.1
		13	1% Chlorhexidine (Cervitec)	NR		NR	-49.7	70
Canali *et al.* 2017[66]	Split-mouth	**19**	Self-Etch Adhesive (Clearfil SE Protect)	179	30	32,5 NR	-39	78
		19	Total Etch Adhesive with Glutaraldehyde (Gluma 2 Bond)				-46	83.6
		20	Resin-Modified GIC (ClinproTM XT)				-50	84.7
Madruga *et al.* 2017[67]	Split-mouth	**20**	Resin-Modified GIC (ClinproTM XT)	70	20	42.7 3 M / 17 W	-42	82.4
		20	Conventional GIC (Vidrion R)	82			-52	86.7
Antoniazzi *et al.* 2014[68]	Parallel	**1**	Placebo Gel	36	107	42.94 55 M / 71 W	-15.6	21.6
		5	2% Sodium Fluoride Gel (Flugel)	37			-30.9	44.3
		5 + 9 + 14	5% NaF, 5% Potassium Oxalate and 10% Strontium Chloride	34			-56.7	75
Tirapelli *et al.* 2011[69]	Parallel	**2**	5% Potassium Nitrate Dentifrice (Sensodyne)	52	120	NR NR	-40	61.5
		15	Sensi Kill®	62			-45	72.6
		15	Bioactive Glass Gel (Biosilicate® gel)	59			-34	49.3
		15	Bioactive Glass powder (Biosilicate® powder)	59			-58	86.6
Hall *et al.* 2017[72]	Parallel	**5**	Dentifrice (Colgate Triple Protection)	45	133	37.4 27 M / 106 W	-17.18	25.8
		11	8% Arginine Calcium Carbonate Dentifrice (Sensitive Pro-Relief)	43			-25.87	41
		15	5% Calcium Sodium Phosphosilicate (CSPS) Dentifrice (Sensodyne ® Repair & Protect)	45			-27.25	39.6
Guentsch *et al.* 2012[73]	Parallel	**12**	Glutaraldehyde (control) (Gluma® Desensitizer)	53	40	34.63 11 M / 29 W	-17	24.3
		25	Biomimetic mineralization system (BIMIN)	58			-28	40
Vano *et al.* 2014[76]	Parallel	**1**	Water (Placebo)	NR	105	42 48 M / 57 W	-3.21	5.6
		5	Fluoride Dentifrice (Colgate Cavity Protection Regular)	NR			-4.66	8.5
		15	15% Nano Hydroxyapatite Dentifrice (PrevDent)	NR			-20.17	35.9
Vano *et al.*	Parallel	**1**	Glycerin (placebo)	NR	105	42	-2.21	4

2018[77]		**5**	NaF Dentifrice (Colgate Cavity Gel) (Positive Control)	NR		40 M / 65 W	-4.79	8.4
		15	2% Nano-hydroxyapatite Dentifrice (Cavex Bite&White)	NR			-18.2	30.5
Litkowski *et al.* 2010[34]	Parallel	**1**	Placebo Dentifrice	NR	66	38.8 12 M / 54 W	-6.8	14
		15	2.5% Novamin Dentifrice	NR			-14.5	28
		15	7.5% Novamin Dentifrice	NR			-21.5	43
Majji *et al.* 2016[79]	Parallel	**2**	5% Potassium Nitrate Dentifrice (RA Thermoseal)	NR	240	20 - 60 93 M / 67 W	-43.3	59.9
		14	3-10% Strontium Chloride Dentifrice (Thermoseal ®)	NR			-43.7	59.9
		15	5% Calcium Sodium Phosphosilicate (Novamin) Dentifrice (Vantej)	NR			-64	88.9
		16	Herbal Dentifrice (Wheezal dental cream)	NR			-35	49.4
Katanec *et al.* 2016[80]	Parallel	**2**	5% Potassium Nitrate Dentifrice (ProSensitive)	NR	74	NR	-25.1	38.1
		5	Dentifrice without Potassium Nitrate (ProSensitive)	NR		NR	-18.6	26.3
Sharma *et al.* 2013[81]	Parallel	**2**	5% KNO3 Dentifrice (Sensodyne® Original)	NR	226	36.3 73 M / 153 W	-22.6	44.3
		5	NaF Dentifrice (Crest Cavity Protection Regular)	NR			-11.6	22.5
		2 + 5	Potassium Oxalate Mouthrinse (Listerine Advanced Defense Sensitive) + NaF Dentifrice (Crest Cavity Protection Regular)	NR			-21.6	42.8
Salian *et al.* 2010[82]	Parallel	**1**	Control Dentifrice (CNR)	NR	30	20 - 50 NR	-2.6	4.6
		2	5% Potassium Nitrate Dentifrice	NR			-11	19.3
		15	5% Calcium Sodium Phosphosilicate Dentifrice (Novamin)	NR			-37.8	65.5
Sharma *et al.* 2010[83]	Parallel	**2**	5% Potassium Nitrate Dentifrice (Sensodent K)	NR	120	31.7 60 M / 60 W	-28.7	49.1
		6	0.4% Stannous Fluoride Dentifrice	NR			-26.5	45.5
		15	7.5% Calcium Sodium Phosphosilicate (Novamin) Dentifrice (Soothe RX)	NR			-39.3	68.6
Hughes *et al.* 2010[85]	Parallel	**8**	8% Strontium Acetate Dentifrice (Sensodyne Rapid Relief)	NR	78	26.45 37 M / 41 W	-17.3	40.1
		11	8% Arginine Calcium Carbonate Dentifrice (Colgate Sensitive Pro-Relief)	NR			-15.7	36.2
Ko *et al.* 2014[86]	Parallel	**22**	LASER Toothbrush (635 nm e 6 mW)	NR	86	40.65 29 M / 57 W	-35	60.3
		25	LED Toothbrush (635 nm e12.9 µW)	NR			-9	14.1
Azarpazhooh *et al.* 2009[87]	Parallel	**1**	Air Delivery (Control)	35	35	32.29 17 M / 18 W	-18.53	36.7
		17	Ozone Delivery	56			-12.91	25.5
Wang *et al.* 2016[88]	Parallel	**5**	NaF Varnish 22600 ppm F (Duraphat)	45	28	18 - 60 7 M / 21 W	-28.1	NC
		11	8% Arginine Calcium Carbonate Dentifrice (Pro-Relief)	26			-41.3	NC
		2 + 5 + 15	20% Hydroxyapatite and Potassium Nitrate, NaF Dentifrice 9000 ppm F (Desensitize Nano-P)	30			-40.8	NC
		2 + 5 + 15	10% Hidroxyapatite, Potassium Nitrate, NaF Dentifrice 900 ppm F (experimental home-care paste)	22			-44.8	NC
Dantas *et al.* 2016[71]	Split-mouth	**5**	5% NaF varnish (Fluorniz®)	40	NR	NR	-35.5	81.1
		22	Low-level laser radiation 4J/cm2	46		NR	-28	67.1

Parkinson *et al.* 2015[89]	Parallel	**5**	0,76% Sodium Monofluorphosphate Dentifrice (Colgate Cavity Protection)	NR	113	42.65 27 M / 92 W	-8.06		13.8
		6	0,454% Stannous Fluoride Dentifrice	NR			-20.2		34.7
Young *et al.* 2016[90]	Parallel	**5 + 15**	5% Calcium Sodium Phosphosilicate and 1426 ppm fluoride as NaF (GSKCH)	NR	296	41.8 51 M / 253 W	-12.59		23.7
		5 + 15	5% Calcium Sodium Phosphosilicate and 1426 ppm fluoride as SMFP (Sensodyne Repair and Protect)	NR			-14.88		26.6
Ding *et al.* 2014[27]	Split-mouth	**1**	Warm water (placebo)		31	46.9 13 M / 18 W		NS VNR	
		12	Gulma Dentin Desensitizer	119				SS VNR	
		20	Clinpro XT Varnish					SS VNR	
Han *et al.* 2017[74]	Parallel	**9**	BisBlock	43	64	46.4 27 M / 37 W	-28.2		45,0
		9	SuperSeal	45			-31.5		45.5
		12 + 24	Gluma Desensitizer	45			-29.3		46.6
		15	DeSen	30			-11.7		18.7
		5 + 24	Hurriseal Dentin Desensitizer	52			-24.6		38.6
Zang *et al.* 2016[33]	Parallel	**5**	Dentifrice containing 1400ppm fluoride as AMFP (Chinese Colgate Triple Protection)	NR	133	40.76 17 M / 117 W		SS VNR	
		15	2,5 % CSPS (4µm) and 1450 ppm fluoride as NaF	NR				SS VNR	
		15	5 % CSPS (4µm) and 1450 ppm fluoride as NaF	NR				SS VNR	
		15	5 % CSPS (14µm) and 1450 ppm fluoride as NaF (Novamin)	NR				SS VNR	
		15	5 % CSPS (14µm) and 1450 ppm fluoride as NaF (UK Sensodyne Repair and Protect)	NR				SS VNR	
Kumar *et al.* 2018[21]	Parallel	**11**	8.0% arginine-calcium carbonate (Colgate® Sensitive Pro-ReliefTM)	NR	80	21 - 68 35 M / 45 W		SS VNR	
		10 + 11	8.0% arginine-calcium carbonate (Colgate® Sensitive Pro-ReliefTM) + iontophoresis	NR				SS VNR	
Konekeri *et al.* 2015[28]	Parallel	**2**	Potassium nitrate dentifrice	NR	48	18 - 67		SS VNR	
		25	10 % Casein Phosphopeptide-Amorphius calcium phosphate	NR		NR		SS VNR	
Mehta *et al.* 2015[31]	Split-mouth	**1**	Distilled Water (Placebo)		35	33.3 10 M / 25 W		SS VNR	
		15	Teethmate AP					SS VNR	
Mehta *et al.* 2014[30]	Parallel	**12**	Glutaraldehyde (Gluma Desensitizer Power Gel)	NR	49	NR 16 M / 34 W		SS VNR	
		15	Teethmate Desensitizer	NR				SS VNR	
		21	NanoSeal	NR				SS VNR	
		21	MS Coat One F	NR				SS VNR	
Lopes *et al.* 2013[29]	Split-mouth	**12**	Glutaraldehyde (Gluma Desensitizer)	11	24	NR NR		SS VNR	
		22	Nd:YAG Laser 1.5W, 10Hz, 100mJ	11				SS VNR	
		12 + 22	Nd:YAG Laser + Gluma De- sensitizer	11				SS VNR	

M: men; **W:** women; **NR:** not reported; **NC:** not calculated; **CNR:** composition not reported; **SS:** statistically significant; **NS:** not statistically significant; **VNR:** values not reported; ***** medium of the 4 quadrants values

Table 3.5 - Summary of the included studies on systematic review from 1 to 3 months

Author (year)	Study design	Treatment Code	Treatment	Number of teeth	Number of subjects	Mean age/age range and Gender	Mean difference of pain assessment between baseline and follow-up	Percentage of DH reduction between baseline and final follow-up
Yilmaz *et al.* 2011[37]	Split-mouth	**1**	NaF Placebo	64	48	41 22 M / 26W	-3	4.6
		1	LASER Placebo	64			-0.3	0.5
		5	NaF Varnish	58			-38.4	56.8
		22	GaAlAs Diode LASER 500mW 810 nm	58			-51.4	81.6
Brahmbhatt *et al.* 2012[20]	Split-mouth	**1**	Iontophoresis Water (placebo) (Desensitron II)	70	25	20-50 NR	NR	0
		5	2% Sodium Fluoride Solution	64			NR	22
		10	Iontophoresis 2% Sodium Fluoride Solution (Desensitron II)	65			NR	74
		12	5% Glutaraldehyde (GLUMA®)	65			NR	52
Vora *et al.* 2012[38]	Split-mouth	**1**	Water (placebo)	150	50	32.4 32 M / 18 W	-29.4	45
		9	Oxalic Acid (BisBlock)				-16	25.7
		12	Glutaraldehyde (Gluma Desensitizer PowerGel)				-45.6	70.6
Bal *et al.* 2015[35]	Split-mouth	**1**	Placebo	22	21	37 5 M / 16 W	2.94	-7.8
		11	8% Arginine Calcium Carbonate Dentifrice (DP) (Colgate Sensitive Pro-Relief)	32			-35.9	65.4
		22	Low Level Laser 685 nm 25 mW (LLL)	41			-34.57	72
		11 + 22	LLL followed by DP	29			-29.98	54.6
		11 + 22	DP followed by LLL	32			-41.85	69.6
Yilmaz *et al.* 2011[41]	Split-mouth	**1**	Control (no treatment)	174	51	44 22 M / 29 W	-5	7.2
		22	Er,Cr:YSGG LASER 2780 nm 0,25W				-62	86.1
		22	GaAlAs Diode LASER 810 nm				-60	84.5
Yilmaz *et al.* 2011[42]	Split-mouth	**1**	LASER Er, Cr:YSGG without emission (Placebo)	146	42	33.8 18 M / 24 W	-7.9	11.5
		22	LASER Er, Cr:YSGG 0,25W				-56.7	80.8
Dilsiz *et al.* 2010[43]	NR	**1**	Not Irradiated (control)	96	24	34 11 M / 13 W	-2.5	3
		22	Er:YAG LASER 2,940-nm				-53.7	64.5
		22	Nd:YAG LASER 1064 nm 1W				-72.5	86.5
		22	GaAlAs Diode LASER 808 nm 100mW				-40.4	48.7
França *et al.* 2015[45]	Parallel	**2**	Potassium nitrate-based toothpaste (Villevie prophylactic paste + Sensodyne Pronamelc, potassium nitrate and sodium fluoride-toothpaste)	NR	50	34.18 13 M / 37 W	-49	62

		11	8% arginine and calcium carbonate (Colgate Sensitive Pro-Relief Toothpaste) + 8% arginine, calcium carbonate and 1,450 ppm fluoride (Colgate Sensitive Pro-Relief Desensitizing Paste with Pro-Arginine Technology)				-57	72,2
Dilsiz *et al.* 2010[46]	NR	**3**	3.75% Potassium Chloride Dentifrice (Sensodyne F)	26	13	31.2 6 M / 7 W	-38.9	48.4
		3 + 22	Erbium and Diode LASER 100 mW 808 nm + 3.75% Potassium Chloride Dentifrice (Sensodyne F)	26			-60	74.3
Osmari *et al.* 2018[47]	Split-mouth	**5**	5% NaF Varnish (Duraphat)	76	19	NR 6 M / 13 W	-34.37	60.1
		9	3% Potassium Oxalate Gel (Oxa-Gel)				-30.58	53.3
		19	Self-Etch Adhesive (Clearfil SE Bond)				-24.37	50.7
		22	High Intensity Diode LASER 810–830 nm 0.5–4.5 W				-34.07	61.7
Pinna *et al.* 2015[50]	Split-mouth	**5**	4 a 6 % NaF Varnish (Flor-Opal® Varnish)	31	46	NR 19 M / 27 W	-10	25
		18	Flow Resin (Vertice Flow)	28			-20	50
		19	Adhesive (Clearfil Protect Bond)	30			-20	50
		21	Sealant (Universal Dentine Sealant)	27			-30	60
Talesara *et al.* 2014[61]	Split-mouth	**9**	Potassium Binoxalate Gel (D/Sens Crystal)	40	20	25 - 55 10 M / 10 W	-70	89.7
		22	Nd:YAG LASER, 1W	40			-69.2	93.5
Patil *et al.* 2015[62]	Parallel	**12**	Glutaraldehyde (Gluma Desensitizer)	18	20	18 - 35 8 M / 12 W	-64	87.7
		19	Universal Adhesive (Single Bond Universal)	18			-54	73
		12 + 19	Glutaraldehyde with Adhesive (Gluma Comfort Bond + Gluma Desensitizer)	18			-65	89
Lopes *et al.* 2015[64]	Split-mouth	**12**	Glutaraldehyde (Gluma Desensitizer)	11	27	22 - 53 NR	-43.71	93
		22	Low Power Laser Low Dose 30mW 810 nm (LPLLD)	11			-21.42	89
		22	Low Level Laser High Dose 100mW 810 nm (LPLHD)	11			-27.38	74
		22 + 12	LPLLD + Glutaraldehyde (Gluma Desensitizer)	11			-53.07	87
		22 + 12	LPLHD + Glutaraldehyde (Gluma Desensitizer)	11			-52	80
Sethna *et al.* 2011[65]	Split-mouth	**12**	5% Glutaraldehyde (Gluma Desensitizer)	NR	250	20 - 55	-39.4	57.2
		13	1% Chlorhexidine (Cervitec)	NR		NR	-52.9	74.5
Canali *et al.* 2017[66]	Split-mouth	**19**	Self-Etch Adhesive (Clearfil SE Protect)	179	30	32,5 NR	-40	80
		19	Total Etch Adhesive with Glutaraldehyde (Gluma 2 Bond)				-45	81.8
		20	Resin-Modified GIC (ClinproTM XT)				-49	83.1
Madruga *et al.* 2017[67]	Split-mouth	**20**	Resin-Modified GIC (ClinproTM XT)	70	20	42.7 3 M / 17 W	-45	88.2
		20	Conventional GIC (Vidrion R)	82			-55	91.7
Tirapelli *et al.* 2011[69]	Parallel	**2**	5% Potassium Nitrate Dentifrice (Sensodyne)	52	120	NR NR	-41	63.1
		15	Sensi Kill®	62			-54	87.1
		15	Bioactive Glass Gel (Biosilicate® gel)	59			-38	55.1
		15	Bioactive Glass powder (Biosilicate® powder)	59			-64	95.5
Hall *et al.*	Parallel	**5**	Dentifrice (Colgate Triple Protection)	45		37.4	-28.48	42.8

2017[72]		**11**	8% Arginine Calcium Carbonate Dentifrice (Sensitive Pro-Relief)	43	133	27 M / 106 W	-38.71	61.3
		15	5% Calcium Sodium Phosphosilicate (CSPS) Dentifrice (Sensodyne® Repair & Protect)	45			-40.67	59.1
Guentsch *et al.* 2012[73]	Parallel	**12**	Glutaraldehyde (control) (Gluma® Desensitizer)	53	40	34.63 11 M / 29 W	-23	32.9
		25	Biomimetic mineralization system (BIMIN)	58			-23	32.9
Pradeep *et al.* 2012[91]	Parallel	**1**	Placebo Dentifrice	NR	149	39.85 27 M / 77 W	-17.6	33.1
		2	5% Potassium Nitrate Dentifrice (SHY)	NR			-31.3	57.1
		7	3.85% Amine Fluoride Dentifrice (AMFLOR)	NR			-33.7	61.7
		15	5% Calcium Sodium Phosphosilicate Dentifrice (SHY-NM)	NR			-36.7	66.1
Pradeep *et al.* 2010[75]	Parallel	**1**	Placebo Dentifrice	NR	110	39.4 58 M / 52 W	-25.7	40.2
		2	5% Potassium Nitrate Dentifrice (SHY)	NR			-29.1	44.3
		15	5% Calcium Sodium Phosphosilicate Dentifrice (SHY-NH)	NR			-52	72.5
Du Min *et al.* 2008[78]	Parallel	**1**	Negative Control Dentifrice Without NovaMin	NR	71	44.1 34 M / 41 W	NR	21.3
		14	Strontium Chloride Dentifrice (Leng Suan Ling Toothpaste)	NR			NR	10.9
		15	5% NovaMin Dentifrice	NR			NR	34.8
Litkowski *et al.* 2010[34]	Parallel	**1**	Placebo Dentifrice	NR	66	38.8 12 M / 54 W	-14.5	28
		15	2.5% Novamin Dentifrice	NR			-15.5	30
		15	7.5% Novamin Dentifrice	NR			-27.4	55
Majji *et al.* 2016[79]	Parallel	**2**	5% Potassium Nitrate Dentifrice (RA Thermoseal)	NR	240	20 - 60 93 M / 67 W	-8.5	11.8
		14	3-10% Strontium Chloride Dentifrice (Thermoseal ®)	NR			-19.2	26.3
		15	5% Calcium Sodium Phosphosilicate (Novamin) Dentifrice (Vantej)	NR			-30.2	41.9
		16	Herbal Dentifrice (Wheezal dental cream)	NR			-8.5	12
Sharma *et al.* 2010[83]	Parallel	**2**	5% Potassium Nitrate Dentifrice (Sensodent K)	NR	120	31.7 60 M / 60 W	-49	83.8
		6	0.4% Stannous Fluoride Dentifrice	NR			-50.8	87.1
		15	7.5% Calcium Sodium Phosphosilicate (Novamin) Dentifrice (Soothe RX)	NR			-50	87.3
Gibson *et al.* 2013[84]	Parallel	**5**	Non-desensitizing Toothpaste (Colgate Cavity Protection Regular)	NR	72	48.21 19 M / 53 W	-6.22	11
		21	Desensitizing Agent (Seal and Protect, Dentsply)	NR			-51.41	83.8
		23	Desensitizing Toothpaste (Colgate Sensitive Fresh Stripe)	NR			-25.04	44.3
Hughes et al. 2010[85]	Parallel	**8**	8% Strontium Acetate Dentifrice (Sensodyne Rapid Relief)	NR	78	26.45 37 M / 41 W	-25.4	58.9
		11	8% Arginine Calcium Carbonate Dentifrice (Colgate Sensitive Pro-Relief)	NR			-21	48.4
Azarpazhooh *et al.* 2009[87]	Parallel	**1**	Air Delivery (Control)	35	35	32.29 17 M / 18 W	-27.66	54.8
		17	Ozone Delivery	56			-27.79	54.9

Wang *et al.* 2016[88]	Parallel	**5**	NaF Varnish 22600 ppm F (Duraphat)	45	28	18 - 60 7 M / 21 W	-25.3	NC
		11	8% Arginine Calcium Carbonate Dentifrice (Pro-Relief)	26			-52.1	NC
		2 + 5 + 15	20% Hydroxyapatite and Potassium Nitrate, NaF Dentifrice 9000 ppm F (Desensitize Nano-P)	30			-45.2	NC
		2 + 5 + 15	10% Hydroxyapatite, Potassium Nitrate, NaF Dentifrice 900 ppm F (experimental home-care paste)	22			-47.3	NC
Parkinson *et al.* 2015[89]	Parallel	**5**	0,76% Sodium Monofluorphosphate Dentifrice (Colgate Cavity Protection)	NR	113	42.65 27 M / 92 W	-14.58	25
		6	0,454% Stannous Fluoride Dentifrice	NR			-36.4	62.5
Young *et al.* 2016[90]	Parallel	**5 + 15**	5% Calcium Sodium Phosphosilicate and 1426 ppm fluoride as NaF (GSKCH)	NR	296	41.8 51 M / 253 W	-22.04	41.4
		5 + 15	5% Calcium Sodium Phosphosilicate and 1426 ppm fluoride as SMFP (Sensodyne Repair and Protect)	NR			-24.47	43.8
Kumari *et al.* 2016[92]	Parallel	**1**	Placebo Dentifrice	NR	120	25 - 60 73 M / 72 W	-11.3	14.4
		2	5% Potassium Nitrate Dentifrice	NR			-44	55.5
		2 + 16	Herbal Dentifrice with Potassium Nitrate and Spinacia oleracia	NR			-42.7	52.7
Kumari *et al.* 2013[93]	Parallel	**1**	Placebo Dentifrice	NR	60	42.1 33 M / 27 W	-9.6	13.5
		16	Herbal Dentifrice Potassium Nitrate and Spinacia oleracia (Hi Ora K)	NR			-34	46.1
Amaechi *et al.* 2018[94]	Parallel	**1**	Control cream without nano-HAP	NR	198	47.61 46 M / 152 W	NR	50.67
		1	Control toothpaste without nano-HAP	NR			NR	47.19
		5	Toothpaste containing 1500 ppm fluoride as MFP	NR			NR	51.59
		15	Toothpaste containing Novamin® technology	NR			NR	51.44
		15	Toothpaste with nano-HAP (high concentration)	NR			NR	41.59
		15	Toothpaste with nano-HAP (low concentration)	NR			NR	38.64
		15	Toothpaste with nano-HAP (medium concentration)	NR			NR	58.65
		15	Cream with nano-HAP (higher concentration)	NR			NR	38.99
		2 + 15	Toothpaste with nano-HAP and (Potassium Nitrate) KNO3	NR			NR	53.16
Kashyap *et al.* 2012[95]	Parallel	**5**	Pepsodent toothpaste	NR	30	18 – 65 NR	-14.94	29.8
		15	SHY NM™ tooth paste with 5% calcium sodium phosphosilicate	NR			-22.27	38.8
Ehlers *et al.* 2012[96]	Split-mouth	**12**	Glutaraldehyde (Gluma Desensitizer)	88	22	39 7 M / 15 W	-38	84.4
		22	LASER Er:YAG 655 nm/1 mW	62			-39	86.7
Han *et al.* 2017[74]	Parallel	**9**	BisBlock	43	64	46.4 27 M / 37 W	-27.2	43.4
		9	SuperSeal	45			-29.3	42.3
		12 + 24	Gluma Desensitizer	45			-26.5	42.1
		15	DeSen	30			-13.3	21.3

		5 + 24	Hurriseal Dentin Desensitizer	52			-21.5	33.7
Zang et al. 2016[33]	Parallel	**5**	Dentifrice containing 1400ppm fluoride as AMFP (Chinese Colgate Triple Protection)	NR	133	40.76 17 M / 117 W	SS VNR	
		15	2,5 % CSPS (4µm) and 1450 ppm fluoride as NaF	NR			SS VNR	
		15	5 % CSPS (4µm) and 1450 ppm fluoride as NaF	NR			SS VNR	
		15	5 % CSPS (14µm) and 1450 ppm fluoride as NaF (Novamin)	NR			SS VNR	
		15	5 % CSPS (14µm) and 1450 ppm fluoride as NaF (UK Sensodyne Repair and Protect)	NR			SS VNR	
Konekeri *et al.* 2015[28]	Parallel	**2**	Potassium nitrate dentifrice	NR	48	18 - 67	SS VNR	
		25	10 % Casein Phosphopeptide-Amorphius calcium phosphate	NR		NR	SS VNR	
Mehta *et al.* 2015[31]	Split-mouth	**1**	Distilled Water (Placebo)	NR	35	33.3 10 M / 25 W	SS VNR	
		15	Teethmate AP	NR			SS VNR	
Mehta *et al.* 2014[30]	Parallel	**12**	Glutaraldehyde (Gluma Desensitizer Power Gel)	NR	49	NR 16 M / 34 W	SS VNR	
		15	Teethmate Desensitizer	NR			SS VNR	
		21	NanoSeal	NR			SS VNR	
		21	MS Coat One F	NR			SS VNR	
Lopes *et al.* 2013[29]	Split-mouth	**12**	Glutaraldehyde (Gluma Desensitizer)	11	24	NR NR	SS VNR	
		22	Nd:YAG Laser 1.5W, 10Hz, 100mJ	11			SS VNR	
		12 + 22	Nd:YAG Laser + Gluma De- sensitizer	11			SS VNR	

M: men; **W:** women; **NR:** not reported; **NC:** not calculated; **CNR:** composition not reported; **SS:** statistically significant; **NS:** not statistically significant; **VNR:** values not reported; ***** medium of the 4 quadrants values

Table 3.6 - Summary of the included studies on systematic review from 3 to 6 months

Author (year)	Study design	Treatment Code	Treatment	Number of teeth	Number of subjects	Mean age/age range and Gender	Mean difference of pain assessment between baseline and follow-up	Percentage of DH reduction between baseline and final follow-up
Yilmaz *et al.* 2011[37]	Split-mouth	**1**	NaF Placebo	64	48	41 22 M / 26W	-1.7	2.6
		1	LASER Placebo	64			-0.6	1.0
		5	NaF Varnish	58			-33.5	49.6
		22	GaAlAs Diode LASER 500mW 810 nm	58			-51.6	81.9
Vora *et al.* 2012[38]	Split-mouth	**1**	Water (placebo)	150	50	32.4 32 M / 18 W	-26	39.8
		9	Oxalic Acid (BisBlock)				-15.6	25.1
		12	Glutaraldehyde (Gluma Desensitizer PowerGel)				-42.4	65.6
Femiano *et al.* 2013[51]	Split-mouth	**5**	2% NaF solution	65	24	38 8 M / 16 W	-3	4.7
		12	Glutaraldehyde (Gluma desensitizer)	67			-18	27.3
		22	Diode LASER 320 nm	69			-34	47.2
		5 + 22	NaF + Diode LASER	61			-42	60.9
Talesara *et al.* 2014[61]	Split-mouth	**9**	Potassium Binoxalate Gel (D/Sens Crystal)	40	20	25 - 55 10 M / 10 W	-75.2	96.4
		22	Nd:YAG LASER, 1W	40			-72.4	97.8
Lopes *et al.* 2015[64]	Split-mouth	**12**	Glutaraldehyde (Gluma Desensitizer)	11	27	22 - 53 NR	-30.55	65
		22	Low Power Laser Low Dose 30mW 810 nm (LPLLD)	11			-16.69	71
		22	Low Level Laser High Dose 100mW 810 nm (LPLHD)	11			-32.19	87
		22 + 12	LPLLD + Glutaraldehyde (Gluma Desensitizer)	11			-49.41	81
		22 + 12	LPLHD + Glutaraldehyde (Gluma Desensitizer)	11			-53.95	83
Canali *et al.* 2017[66]	Split-mouth	**19**	Self-Etch Adhesive (Clearfil SE Protect)	179	30	32,5 NR	-39	78
		19	Total Etch Adhesive with Glutaraldehyde (Gluma 2 Bond)				-46	83.6
		20	Resin-Modified GIC (ClinproTM XT)				-52	88.1
Madruga *et al.* 2017[67]	Split-mouth	**20**	Resin-Modified GIC (ClinproTM XT)	70	20	42.7 3 M / 17 W	-47	92.2
		20	Conventional GIC (Vidrion R)	82			-58	96.7
Tirapelli *et al.* 2011[69]	Parallel	**2**	5% Potassium Nitrate Dentifrice (Sensodyne)	52	120	NR	-47	72.3
		15	Sensi Kill®	62			-55	88.7
		15	Bioactive Glass Gel (Biosilicate® gel)	59		NR	-38	55.1
		15	Bioactive Glass powder (Biosilicate® powder)	59			-66.1	98.7
Jalali *et el.* 2010[70]	Parallel	**4**	Varnish Containing Potassium Fluoride (VivaSens)	111	27	38 NR	-21.75*	63.5*
		21	Resin-based Sealing Material (Seal and Protect)	103			-17.75*	61.7*
Gibson *et al.* 2013[84]	Parallel	**5**	Non-desensitizing Toothpaste (Colgate Cavity Protection Regular)	NR	72	48.21 19 M / 53 W	-8.52	15.1
		21	Desensitizing Agent (Seal and Protect, Dentsply)	NR			-53.58	87.4

		23	Desensitizing Toothpaste (Colgate Sensitive Fresh Stripe)	NR			-27.5		48.7
Ehlers *et al.* 2012[96]	Split-mouth	**12**	Glutaraldehyde (Gluma Desensitizer)	88	22	39	-44		97.8
		22	LASER Er:YAG 655 nm/1 mW	62		7 M / 15 W	-40		88.9
Raichur *et al.* 2012[32]	Parallel	**2**	5% Potassium Nitrate Gel	NR	54	25-45 30 M / 24 W		SS VNR	
		6	0,4 % Stannous fluoride gel	NR				SS VNR	
		22	LASER GaAlAs 940nm DL	NR				SS VNR	
Mehta *et al.* 2015[31]	Split-mouth	**1**	Distilled Water (Placebo)	NR	35	33.3 10 M / 25 W		SS VNR	
		15	Teethmate AP	NR				SS VNR	
Mehta *et al.* 2014[30]	Parallel	**12**	Glutaraldehyde (Gluma Desensitizer Power Gel)	NR	49	NR 16 M / 34 W		SS VNR	
		15	Teethmate Desensitizer	NR				SS VNR	
		21	NanoSeal	NR				SS VNR	
		21	MS Coat One F	NR				SS VNR	
Lopes *et al.* 2013[29]	Split-mouth	**12**	Glutaraldehyde (Gluma Desensitizer)	11	24	NR NR		SS VNR	
		22	Nd:YAG Laser 1.5W, 10Hz, 100mJ	11				SS VNR	
		12 + 22	Nd:YAG Laser + Gluma De- sensitizer	11				SS VNR	

M: men; **W:** women; **NR:** not reported; **NC:** not calculated; **CNR:** composition not reported; **SS:** statistically significant; **NS:** not statistically significant; **VNR:** values not reported; ***** medium of the 4 quadrants values

Table 3.7 - Summary of the included studies on systematic review of more than 6 months

Author (year)	Study design	Treatment Code	Treatment	Number of teeth	Number of subjects	Mean age/age range and Gender	Mean difference of pain assessment between baseline and follow-up	Percentage of DH reduction between baseline and final follow-up
Talesara *et al.* 2014[61]	Split-mouth	**9**	Potassium Binoxalate Gel (D/Sens Crystal)	40	20	25 - 55 10 M / 10 W	-52.4	67.2
		22	Nd:YAG LASER, 1W	40			-58.8	79.5
Lopes e*t al.* 2017[63]	Split-mouth	**12**	Glutaraldehyde (Gluma Desensitizer)	13	32	22 - 53 NR	-47	100
		22	LASER Low Power Low Dose (LPLD) 810 nm 30 mW	13			-14	59.6
		22	LASER Low Power High Dose (LPHD) 810nm 100 mW	13			-29.5	79.7
		22	Nd:YAG LASER 1064 nm 1 W	13			-25	54.3
		22 + 22	LPLD + Nd:YAG LASER 1064 nm	13			-31.5	74.1
		22 + 22	LPHD + Nd:YAG LASER 1064 nm	13			-54.5	89.3
		12 + 22	LPLD + Glutaraldehyde (Gluma Desensitizer)	13			-60	98.4
		12 + 22	LPHD + Glutaraldehyde (Gluma Desensitizer)	13			-46	70.8
		22 + 12	Nd:YAG LASER + Glutaraldehyde (Gluma Desensitizer)	13			-46	78
Guentsch *et al.* 2012[73]	Parallel	**12**	Glutaraldehyde (Gluma® Desensitizer)	53	40	34.63 11 M / 29 W	-20	28.6
		25	Biomimetic mineralization system (BIMIN)	58			-21	30

M: men; **W:** women; **NR:** not reported; **NC:** not calculated; **CNR:** composition not reported; **SS:** statistically significant; **NS:** not statistically significant; **VNR:** values not reported; ***** medium of the 4 quadrants values

Table 4 – *P* values referent to the statistical comparison between DH reduction of each treatment *versus* the placebo at the different time points.

	Treatment	1 day	2 -7 days	8 -15 days	15 days – 1 month	1 – 3 months
2	Potassium nitrate	1.000	0.372	0.765	0.248	**0.001**
3	Potassium chloride	n.d.	n.d.	n.d.	n.d.	n.d.
4	Potassium fluoride	n.d.	n.d.	n.d.	n.d.	n.d.
5	Sodium fluoride	0.364	0.207	0.156	0.120	0.866
6	Stannous fluoride	1.000	0.998	**0.014**	0.977	0.996
7	Amine fluoride	n.d.	n.d.	n.d.	n.d.	n.d.
8	Strontium acetate	1.000	0.957	n.d.	1.000	n.d.
9	Oxalates	0.194	0.999	0.399	0.995	0.088
10	Iontophoresis	n.d.	n.d.	n.d.	n.d.	n.d.
11	Arginine	0.990	1.000	0.070	0.145	**0.038**
12	Glutaraldehyde + HEMA	**< 0.001**	**0.015**	n.d.	**< 0.001**	**0.002**
13	Chlorhexidine	n.d.	n.d.	n.d.	n.d.	n.d.
14	Strontium Chloride	n.d.	n.d.	n.d.	n.d.	n.d.
15	Hydroxyapatite	n.d.	0.804	**0.010**	**0.008**	**< 0.001**
16	Herbal	n.d.	n.d.	n.d.	n.d.	0.139
17	Ozone	n.d.	n.d.	n.d.	n.d.	n.d.
18	Composite resins	0.577	0.889	n.d.	0.482	n.d.
19	Adhesive systems	0.063	0.950	0.987	0.168	**0.027**
20	Glass ionomer cements	**0.012**	0.127	**0.001**	**0.003**	**0.002**
21	Dentin sealants	n.d.	0.962	n.d.	n.d.	0.195
22	Laser	**0.002**	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**
23	Potassium Citrate	n.d.	n.d.	n.d.	n.d.	n.d.
24	HEMA	n.d.	n.d.	n.d.	n.d.	n.d.
25	Others	n.d.	n.d.	n.d.	n.d.	n.d.

n.d.: not determined due to insufficient number of studies found in the literature. In the cases where statistical significance was found, DH decrease was always superior in the treatment groups.

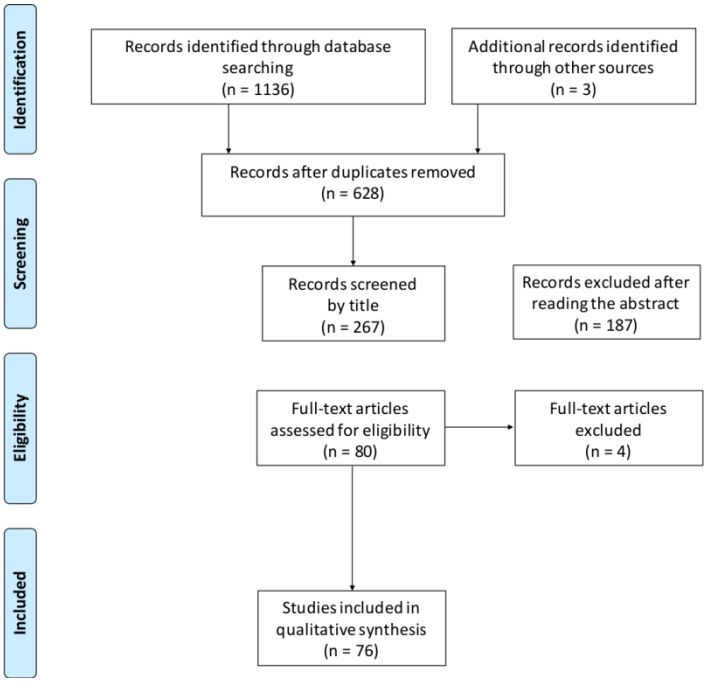
Figure legends

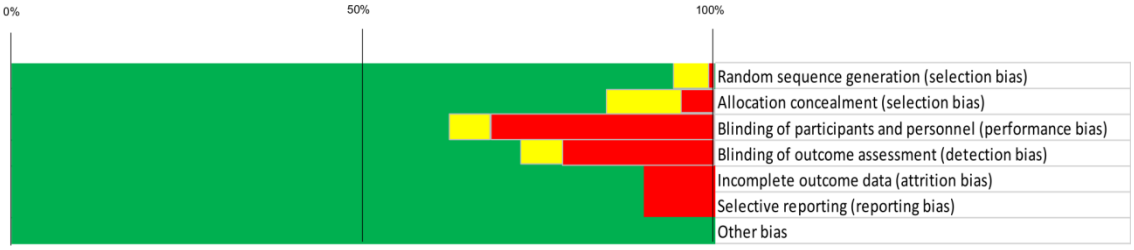
Figure 1 – PRISMA flow diagram of the study selection

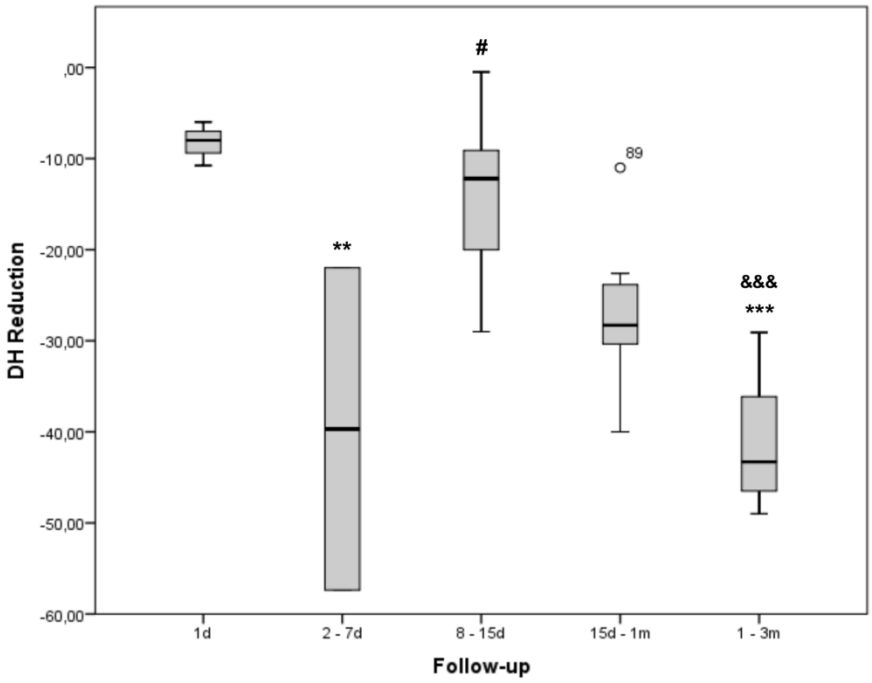
Figure 2 – Summary of methodological quality assessment of the RCT studies of the systematic review

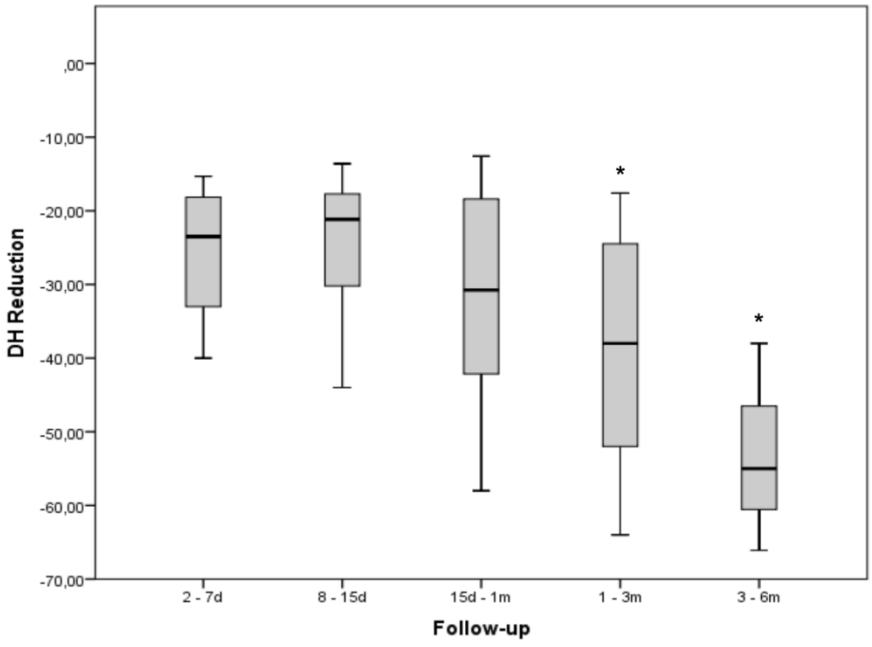
Figure 3 – Hypersensitivity reduction with potassium nitrate treatment over time. The results were expressed in median and minimum and maximum value. (* statistical differences compared to day 1 follow-up; # statistical differences compared to days 2-7 follow-up; $ statistical differences compared to days 8-15 follow-up; O Outlier). Different levels of significance: 1 symbol – $p < 0.05$; 2 symbols – $p < 0.01$; 3 symbols – $p < 0.001$

Figure 4 – Hypersensitivity reduction with hydroxyapatite treatment over time. The results were expressed in median and minimum and maximum value. (* statistical differences compared to days 8-15 follow-up). Different levels of significance: 1 symbol – $p < 0.05$; 2 symbols – $p < 0.01$; 3 symbols – $p < 0.001$

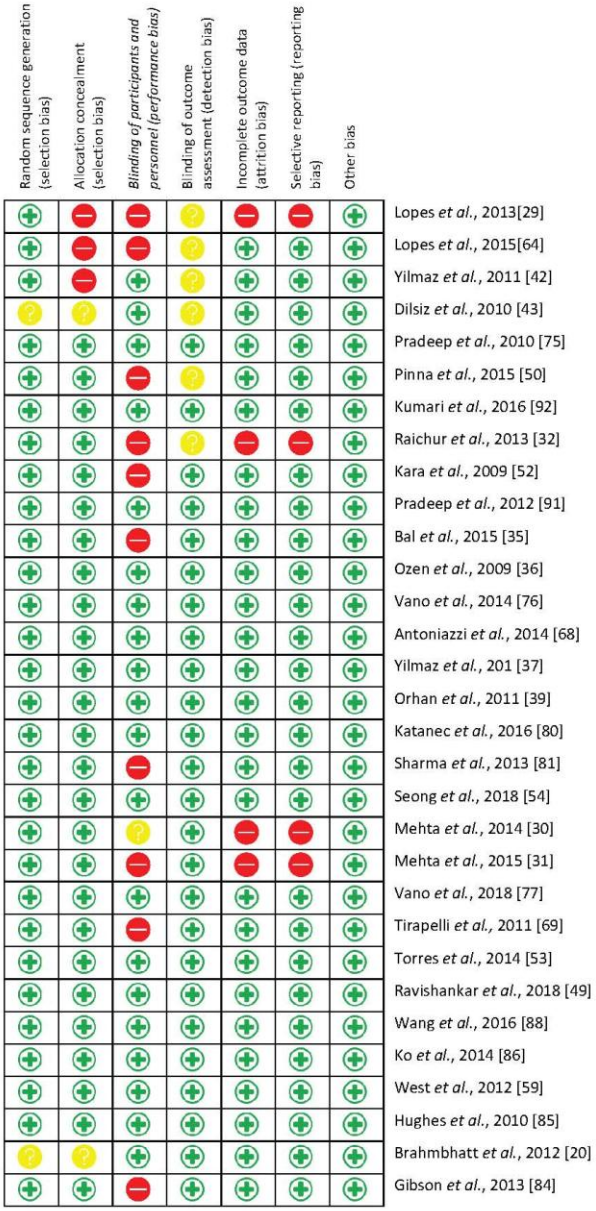


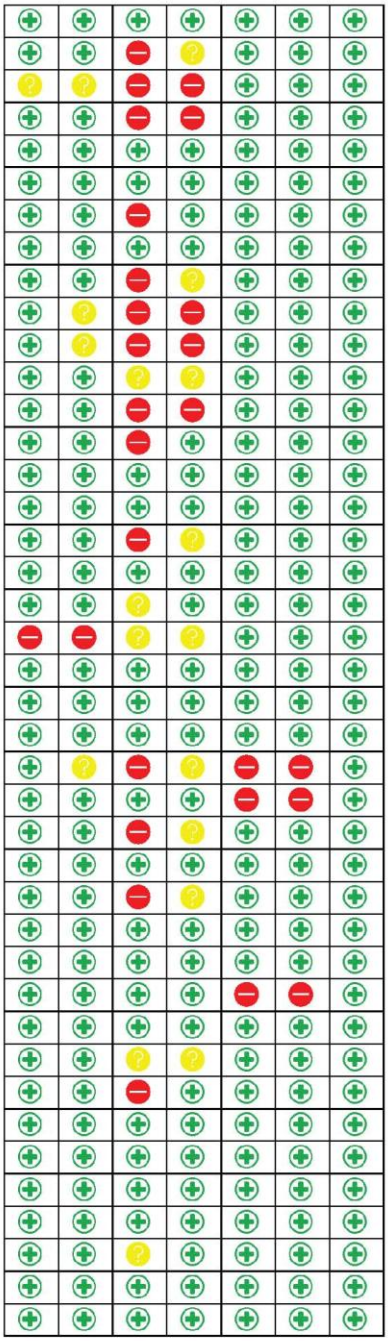






Appendix 1 - Evaluation of quality assessment of RCT studies of the systematic review.





Appendix 2 – *P* values referent to the statistical comparison between DH reduction of each treatment at the different time points.

Code	*Treatment*	*P value*
1	Placebo	0.435
2	Potassium nitrate	**0.001**
3	Potassium chloride	n.d.
4	Potassium fluoride	n.d.
5	Sodium fluoride	n.d.
6	Stannous fluoride	0.248
7	Amine fluoride	n.d.
8	Strontium acetate	0.180
9	Oxalates	0.816
10	Iontophoresis	n.d.
11	Arginine	0.130
12	Glutaraldehyde + HEMA	0.978
13	Chlorhexidine	n.d.
14	Strontium Chloride	n.d.
15	Hydroxyapatite	**0.018**
16	Herbal	n.d.
17	Ozone	n.d.
18	Composite resins	0.718
19	Adhesive systems	0.197
20	Glass ionomer cements	0.650
21	Dentin sealants	0.718
22	Laser	0.107
23	Potassium Citrate	n.d.
24	HEMA	n.d.
25	Others	n.d.

n.d.: not determined due to insufficient number of studies found in literature. In the cases where statistical significance was found, DH decrease was always superior in the treatment groups.