Desensitizing toothpaste versus placebo for dentin hypersensitivity: a systematic review and meta-analysis


Abstract

Aim: The aim is to assess the effect of desensitizing toothpaste on dentin hypersensitivity.

Methods: We searched PubMed, CENTRAL, and Embase on December 20, 2013.

Results: Out of the 626 articles searched, a total of 31 randomized controlled clinical trials were included. The Standardized mean differences (SMD) for potassium-containing toothpaste (n = 8) was −1.28 (95% Confidence interval (CI) −2.05 to −0.51; I² = 93%); Stannous fluoride- (n = 6) was −1.37 (95% CI, −2.30 to −0.44; I² = 95%); Potassium and stannous fluoride- (n = 3) was −2.50 (95% CI, −4.10 to −0.91; I² = 95%); Calcium sodium phosphosilicate- (n = 4) was −2.36 (95% CI, −3.72 to −1.00; I² = 92%); Arginine- (n = 8) was −3.25 (95% CI, −3.87 to −2.63; I² = 86%). The desensitizing effect was favoured in the intervention group treated with potassium-, stannous fluoride-, potassium and stannous fluoride-, calcium sodium phosphosilicate-, and arginine-containing toothpaste compared to placebo. Whereas, strontium-containing toothpaste (SMD, 0.05; 95% CI, −0.34 to 0.44; I² = 64%) was found to have no statistically significant desensitizing effect in the meta-analysis of four studies.

Conclusions: The study reports that there is sufficient evidence to support the use of potassium-, stannous fluoride-, potassium and stannous fluoride-, calcium sodium phosphosilicate-, and arginine-containing desensitizing toothpastes for dentin hypersensitivity, but not the use of strontium-containing desensitizing toothpaste.

Dentin hypersensitivity is defined as short, sharp pain arising from exposed dentin in response to external stimuli, which are typically thermal, evaporative, tactile, osmotic, or chemical, and which cannot be ascribed to any other form of dental defect or disease (Holland et al. 1997). These symptoms recorded the prevalence ranging from 3% to 73% (Shiau 2012), with higher female incidence than male, commonly affecting premolar and incisor teeth (Addy et al. 1987). It mostly affects patients in their 20s–40s, and the severity can increase due to an increase in periodontal disease, gingival recession, or erosive exposure (Gillam et al. 1999); it can decrease due to the generation of secondary dentin (Cummins 2009). Though the accurate mechanism of dentin hypersensitivity has yet to be identified, it is explained by the hydrodynamic theory suggested by Brannstrom. According to this theory, if the exposed dentin is stimulated, fluid in the dentinal tubule stimulates the...
baroreceptor; thus causing a neural signal and a painful sensation (Brannstrom 1963). Therefore, dentin hypersensitivity can be treated by interrupting neural response for pain stimuli or blocking the exposed dentinal tubules (Cummins 2009). A typical nervous transmission controller is potassium, with strontium salts, oxalates, calcium phosphate, fluorides, formaldehyde, and glutaraldehyde acting as tubule plug. Glass ionomer, composite resin, and dentin adhesive act as the dentin sealer; other methods include laser and mucogingival plastic surgery (Shiau 2012). These treatments can be performed both at home and in office. Using desensitizing toothpaste is a convenient, cost-effective, easy-to-use, and non-invasive method. To date, various desensitizing toothpastes containing potassium, strontium, stannous fluoride, arginine, or sodium calcium phosphosilicate have been developed worldwide.

There is already a published Cochrane systemic review with meta-analysis questioning the efficacy of potassium-containing toothpastes for dentine hypersensitivity as the result of subjective assessment of three trials (Poulsen et al. 2006). It focuses solely on potassium-containing toothpaste and has not been updated since 2006; as such, it is out of date. Another recent study systematically investigated arginine-containing toothpastes and suggested that arginine-containing toothpastes were associated with the reduction in dentin hypersensitivity compared to both placebo and positive control toothpastes (Yan et al. 2013). An up-to-date search including the wide variety of available desensitizing toothpastes is required.

This meta-analysis study, therefore, aimed to investigate the effect of potassium-, stannous fluoride-, potassium and stannous fluoride-, strontium-, calcium sodium phosphosilicate-, and arginine-containing desensitizing toothpaste compared to placebo in the treatment of dentin hypersensitivity as measured by air blast test scores in adult patients suffering from dentin hypersensitivity.

Materials and Methods

This meta-analysis was conducted in agreement with recommendation of the principles of the PRISMA statement (http://www.prisma-statement.org).

Search

We conducted electronic searches in PubMed, Cochrane Central Register of Controlled Trials (CENTRAL) in Cochrane Library, and Embase on December 20, 2013 using common keywords related to the effect of toothpaste on dentin hypersensitivity. The keywords used for the literature search were (toothpaste OR dentifrice) AND (dentin hypersensitivity OR dentin sensitivity). A manual search of the relevant articles (reference list of selected articles) was also applied to identify additional studies. We selected only articles published in English.

Eligibility criteria

We included only randomized controlled clinical trials that had intervention and control groups in human and reported the effect of toothpaste on dentin hypersensitivity. Articles were selected according to the following inclusion criteria. We used PICO (patient, intervention, comparator, outcome) terms: (1) Patient: adult dentin hypersensitivity sufferer, with post-operative (bleaching, periodontal treatment, and restorative treatment) hypersensitivity excluded; (2) Intervention: potassium-, stannous fluoride-, potassium, and stannous fluoride-, strontium-, calcium sodium phosphosilicate-, and arginine-containing desensitizing toothpaste; (3) Comparator: placebo; (4) Outcome: air blast test score [VAS (visual analogue scales), VRS (verbal rating scales), and SCASS (Schiff cold air sensitivity scale)]. The air blast test is a more accurate, physiological, controllable, and reproducible method compared to tactile test, thermal test, or subjective assessment. The PICO question formulated for this study was as follows. “In adults, are desensitizing toothpastes effective for dentin hypersensitivity compared with placebo?” Cases used as positive control to compare with the result of other ingredients were excluded. Case reports, case series, editorials, in vitro studies, animal experiments, unpublished materials, and review papers were excluded.

Study selection and data collection

Two authors (J.H. Bae and Y.K. Kim) independently assessed the eligibility of all studies retrieved from the databases. When there were disagreements between the evaluators concerning the selected studies, such cases were resolved by discussion. From the studies included in the final analysis, we extracted the following data: study name (along with the name of the first author and year of publication), journal name, country, study design, participants, age of participants, details of intervention, follow-up period, pain score type, and values of outcome measurement in both intervention and control groups. Excel was used in study selection and data collection. If the study had more than one follow-up period, we would use the final assessment for data extraction (Lin et al. 2013). Contact with the author of a study was attempted if there was insufficient information in a publication.

Risk of bias assessment

We assessed the quality of the included individual studies based on Cochrane’s collaboration tool for assessing the risk of bias as follows: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias (groups similar at baseline) (Higgins & Green 2011). High quality of evidence was estimated when all domains were at low risk of bias, a moderate quality of evidence was estimated when one or more key domains were at an unclear risk of bias and no risk of bias, and a low quality of evidence was estimated when one or more domains were at a high risk of bias (Higgins & Green 2011).

Statistical analyses

To evaluate if there is a difference in the effect of desensitizing toothpaste on dentin hypersensitivity, we used a standardized mean difference (SMD) with 95% CI. To combine data from different scales, it has been suggested that dividing the mean difference in each study by that study’s standard deviation to create a SMD which
would be comparable across studies (Glass 1976). According to Cohen’s rule of thumb (Cohen 1977), a pooled SMD is interpreted as follows: 0.2 for small effect, around 0.5 for medium effect, and 0.8 or more for large effect. If the 95% CI does not include the value 0, then the pooled SMD is statistically significant ($p < 0.05$).

All the SMD and 95% CIs were calculated on the basis of the random effects model.

Data were analysed using RevMan 5.2 software (The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark).

Power analysis was performed using SAS macro (SAS institute Inc., Cary, NC, USA), with the level of significance set at 0.05.

**Results**

**Study selection**

A total of 626 articles were selected after searching three databases and hand-searching the relevant bibliographies. After excluding 213 duplicate articles and 374 articles that did not satisfy the inclusion criteria mentioned in the Materials and Methods section, we reviewed the full texts of 39 articles. Among those, eight articles were excluded because four articles (Chesters et al. 1992, Salvato et al. 1992, Silverman et al. 1994, Du Min et al. 2008) had insufficient data reported as mean and standard deviation, three articles (Pearce et al. 1994, Conforti et al. 2000, Rajesh et al. 2012) were non-randomized controlled clinical trials and one article (Prasad et al. 2010) had no assessment of the air blast test. Because three articles (Chesters et al. 1992, Salvato et al. 1992, Silverman et al. 1994) out of four that had insufficient information in a publication were written two decades ago, contact with one study author (Du Min et al. 2008) was attempted, but with no reply.

We included a total of 31 randomized controlled clinical trials in the final analysis (Fig. 1).

**Study characteristics**


**Risk of bias assessment**

Twenty-one out of 31 studies were low risk of bias for random sequence generation, 12 studies were low risk of bias for allocation concealment, 28 studies were low risk of bias for blinding of participants and personnel, 27 studies were adequate for free of incomplete outcome data, and 30 studies were adequate for free of other sources of bias (groups similar at baseline); all of the included
Table 1. Characteristics of randomized clinical trials included in the final analysis (n = 31).

<table>
<thead>
<tr>
<th>Study</th>
<th>Journal</th>
<th>Country</th>
<th>Funding source</th>
<th>Age (years)</th>
<th>Intervention</th>
<th>Follow-up period</th>
<th>Pain score type</th>
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<tbody>
<tr>
<td>Potassium-containing toothpaste</td>
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<tr>
<td>Nagata et al. (1994)</td>
<td><em>J Clin Periodontol</em></td>
<td>Japan</td>
<td>Kobayashi pharmaceutical Co.</td>
<td>29–63</td>
<td>5% potassium nitrate</td>
<td>12 weeks</td>
<td>VRS (0–3)</td>
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<tr>
<td>Schiff et al. (1994)</td>
<td><em>J Clin Dent</em></td>
<td>USA</td>
<td>Colgate-Palmolive Co.</td>
<td>20–60</td>
<td>5% potassium nitrate</td>
<td>12 weeks</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>Gillam et al. (1996)</td>
<td><em>J Peridontol</em></td>
<td>UK</td>
<td>SmithKline Beecham Consumer Healthcare</td>
<td>18–60</td>
<td>3.75% potassium chloride</td>
<td>6 weeks</td>
<td>VAS (0–10)</td>
</tr>
<tr>
<td>Silverman et al. (1996)</td>
<td><em>J Am Dent Assoc</em></td>
<td>USA</td>
<td>Procter &amp; Gamble Co</td>
<td>19.5–77.7</td>
<td>5% potassium nitrate</td>
<td>8 weeks</td>
<td>VAS (0–100)</td>
</tr>
<tr>
<td>West et al. (1997)</td>
<td><em>J Clin Periodontol</em></td>
<td>UK</td>
<td>SmithKline Beecham Consumer Healthcare</td>
<td>18–65</td>
<td>Potassium nitrate</td>
<td>6 weeks</td>
<td>VAS (0–10)</td>
</tr>
<tr>
<td>Schiff et al. (1998)</td>
<td><em>J Clin Dent</em></td>
<td>USA</td>
<td>Colgate-Palmolive Co</td>
<td>18–59</td>
<td>5% potassium nitrate</td>
<td>8 weeks</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>Wara-aswapati et al. (2005)</td>
<td><em>J Clin Periodontol</em></td>
<td>Thailand</td>
<td>GlaxoSmithKline (Thailand) Ltd</td>
<td>21–59</td>
<td>5% potassium nitrate</td>
<td>12 weeks</td>
<td>VAS (0–10)</td>
</tr>
<tr>
<td>Kakar &amp; Kakar (2013)</td>
<td><em>Am J Dent</em></td>
<td>India</td>
<td>Colgate-Palmolive Co</td>
<td>18–48</td>
<td>5% potassium nitrate</td>
<td>8 weeks</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>Schiff et al. (2005)</td>
<td><em>Compend Contin Educ Dent</em></td>
<td>USA</td>
<td>Procter &amp; Gamble Co</td>
<td>20–62</td>
<td>0.454% stannous fluoride</td>
<td>8 weeks</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>Schiff et al. (2006)</td>
<td><em>J Contemp Dent Pract</em></td>
<td>USA</td>
<td>Procter &amp; Gamble Co</td>
<td>20–64</td>
<td>0.454% stannous fluoride</td>
<td>8 weeks</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>Day et al. (2010)</td>
<td><em>J Contemp Dent Pract</em></td>
<td>UK</td>
<td>Procter &amp; Gamble Co</td>
<td>18–70</td>
<td>0.45% stannous fluoride</td>
<td>4 weeks</td>
<td>VRS (0–3)</td>
</tr>
<tr>
<td>Chaknis et al. (2011)</td>
<td><em>Am J Dent</em></td>
<td>USA</td>
<td>Colgate-Palmolive Co</td>
<td>18–70</td>
<td>0.45% stannous fluoride</td>
<td>8 weeks</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>He et al. (2011)</td>
<td><em>J Clin Dent</em></td>
<td>USA</td>
<td>Procter &amp; Gamble Co</td>
<td>19–64</td>
<td>0.45% stannous fluoride</td>
<td>2 weeks</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>Parkinson et al. (2013)</td>
<td><em>Am J Dent</em></td>
<td>UK</td>
<td>GlaxoSmithKline Consumer Healthcare</td>
<td>21–65</td>
<td>0.45% stannous fluoride</td>
<td>8 weeks</td>
<td>SCASS (0–3)</td>
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<tr>
<td>Potassium and Stannous fluoride-containing toothpaste</td>
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<tr>
<td>Schiff et al. (2000)</td>
<td><em>Compend Contin Educ Dent Suppl</em></td>
<td>USA</td>
<td>Colgate-Palmolive Co</td>
<td>mean 36, 35</td>
<td>5% potassium nitrate + 0.454% stannous fluoride</td>
<td>8 weeks</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>Sowinski et al. (2000)</td>
<td><em>Compend Contin Educ Dent</em></td>
<td>USA</td>
<td>Colgate-Palmolive Co</td>
<td>18–70</td>
<td>5% potassium nitrate + 0.454% stannous fluoride</td>
<td>8 weeks</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>Sowinski et al. (2001)</td>
<td><em>J Clin Periodontol</em></td>
<td>USA</td>
<td>Colgate-Palmolive Co</td>
<td>18–70</td>
<td>5% potassium nitrate + 0.59% stannous fluoride</td>
<td>8 weeks</td>
<td>SCASS (0–3)</td>
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<tr>
<td>Strontium-containing toothpaste</td>
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<tr>
<td>Gillam et al. (1996)</td>
<td><em>J Peridontal</em></td>
<td>UK</td>
<td>SmithKline Beecham Consumer Healthcare</td>
<td>18–60</td>
<td>8% strontium acetate</td>
<td>6 weeks</td>
<td>VAS (0–10)</td>
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<tr>
<td>West et al. (1997)</td>
<td><em>J Clin Periodontal</em></td>
<td>UK</td>
<td>SmithKline Beecham Consumer Healthcare</td>
<td>18–65</td>
<td>Strontium acetate</td>
<td>6 weeks</td>
<td>VAS (0–10)</td>
</tr>
<tr>
<td>Mason et al. (2010)</td>
<td><em>J Clin Dent</em></td>
<td>UK</td>
<td>GlaxoSmithKline Consumer Healthcare</td>
<td>mean 41.8, 41.4</td>
<td>8% strontium acetate</td>
<td>3 days</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>Li et al. (2011)</td>
<td><em>J Clin Dent</em></td>
<td>USA</td>
<td>Colgate-Palmolive Co</td>
<td>18–69</td>
<td>8% strontium acetate</td>
<td>7 days</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>Calcium sodium phosphosilicate-containing toothpaste</td>
<td></td>
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<tr>
<td>Litkowski &amp; Greenspan (2010)</td>
<td><em>J Clin Dent</em></td>
<td>USA</td>
<td>US Biomaterials</td>
<td>mean 39.2, 36.7</td>
<td>7.5% sodium calcium phosphosilicate</td>
<td>8 weeks</td>
<td>VAS (0–100)</td>
</tr>
<tr>
<td>Study</td>
<td>Journal</td>
<td>Country</td>
<td>Funding source</td>
<td>Age (years)</td>
<td>Intervention</td>
<td>Follow-up period</td>
<td>Pain score type</td>
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<td>Pradeep &amp; Sharma (2010)</td>
<td><em>J Periodontol</em></td>
<td>India</td>
<td>Group Pharmaceuticals</td>
<td>20–60</td>
<td>5% sodium calcium phosphosilicate</td>
<td>6 weeks</td>
<td>VAS (0–10)</td>
</tr>
<tr>
<td>Salian et al. (2010)</td>
<td><em>J Clin Dent</em></td>
<td>India</td>
<td>Group Pharmaceuticals</td>
<td>20–50</td>
<td>5% sodium calcium phosphosilicate</td>
<td>4 weeks</td>
<td>VAS (0–10)</td>
</tr>
<tr>
<td>Pradeep et al. (2012)</td>
<td><em>Aust Dent J</em></td>
<td>India</td>
<td>Group Pharmaceuticals</td>
<td>20–60</td>
<td>5% sodium calcium phosphosilicate</td>
<td>6 weeks</td>
<td>VAS (0–10)</td>
</tr>
<tr>
<td>Ayad et al. (2009)</td>
<td><em>J Clin Dent</em></td>
<td>Canada</td>
<td>Colgate-Palmolive Co.</td>
<td>18–66</td>
<td>8% arginine + calcium carbonate</td>
<td>3 days</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>Nathoo et al. (2009)</td>
<td><em>J Clin Dent</em></td>
<td>USA</td>
<td>Colgate-Palmolive Co.</td>
<td>18–70</td>
<td>8% arginine + calcium carbonate</td>
<td>3 days</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>Fu et al. (2010)</td>
<td><em>Am J Dent</em></td>
<td>China</td>
<td>Colgate-Palmolive Co.</td>
<td>23–70</td>
<td>8% arginine + calcium carbonate</td>
<td>3 days</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>Que et al. (2010)</td>
<td><em>Am J Dent</em></td>
<td>China</td>
<td>Colgate-Palmolive Co.</td>
<td>18–70</td>
<td>8% arginine + calcium carbonate</td>
<td>8 weeks</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>Docimo et al. (2011)</td>
<td><em>J Clin Dent</em></td>
<td>Italy</td>
<td>Colgate-Palmolive Co.</td>
<td>20–69</td>
<td>8% arginine + calcium carbonate</td>
<td>8 weeks</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>Kakar et al. (2012)</td>
<td><em>J Clin Dent</em></td>
<td>India</td>
<td>Colgate-Palmolive Co.</td>
<td>25–56</td>
<td>8% arginine + calcium carbonate</td>
<td>8 weeks</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>Hegde et al. (2013)</td>
<td><em>Am J Dent</em></td>
<td>India</td>
<td>Global health research group</td>
<td>23–61</td>
<td>8% arginine + calcium carbonate</td>
<td>8 weeks</td>
<td>SCASS (0–3)</td>
</tr>
<tr>
<td>Kakar et al. (2013)</td>
<td><em>Am J Dent</em></td>
<td>India</td>
<td>Colgate-Palmolive Co.</td>
<td>21–57</td>
<td>8% arginine + calcium carbonate</td>
<td>8 weeks</td>
<td>SCASS (0–3)</td>
</tr>
</tbody>
</table>

VRS, verbal rating scales; SCASS, Schiff cold air sensitivity scale; VAS, visual analogue scales.
studies were adequate for blinding of outcome assessment and selective outcome reporting (Table 2). Three included studies were of high quality, 23 were moderate, and five were low quality.

**Result of individual studies and synthesis of results**

**Effect of potassium-containing toothpaste on dentin hypersensitivity**

In the meta-analysis of eight studies on potassium-containing toothpaste, the desensitizing effect was favoured in the intervention group treated with potassium-containing toothpaste compared to placebo (SMD, 2.36; 95% CI, −3.72 to −1.00; \( I^2 = 92\% \); Fig. 2).

**Effect of stannous fluoride-containing toothpaste on dentin hypersensitivity**

In the meta-analysis of five studies in this category, the desensitizing effect was favoured in the intervention group treated with stannous fluoride-containing toothpaste compared to placebo (SMD, 0.05; 95% CI, −0.51 to 0.01; \( I^2 = 93\% \); Fig. 2).

**Effect of potassium and stannous fluoride-containing toothpaste on dentin hypersensitivity**

In the meta-analysis of eight studies on potassium and stannous fluoride-containing desensitizing toothpaste, the desensitizing effect was favoured in the intervention group treated with potassium and stannous fluoride-containing toothpaste compared to placebo (SMD, 2.36; 95% CI, −3.72 to −1.00; \( I^2 = 86\% \); Fig. 2).

**Effect of arginine-containing toothpaste on dentin hypersensitivity**

In the meta-analysis of eight studies on arginine-containing desensitizing toothpaste, the desensitizing effect was favoured in the intervention group treated with arginine-containing toothpaste compared to placebo (SMD, 2.36; 95% CI, −3.72 to −1.00; \( I^2 = 86\% \); Fig. 2).

**Discussion**

The current meta-analysis attempted to analyse all published randomized controlled trials and controlled clinical trials to assess the effect of desensitizing toothpaste containing any active agent versus placebo on dentin hypersensitivity as measured by air blast test scores. This study suggests the strong benefit of treating dentin hypersensitivity with potassium-, stannous fluoride-, potassium and stannous fluoride-, calcium sodium phosphosilicate- and arginine-containing desensitizing toothpastes beyond a placebo effect, but not the use of strontium-containing desensitizing toothpaste, which is part of a 99% statistical power. The overall SMD of the effect of potassium-, stannous fluoride-, potassium and stannous fluoride-, calcium sodium phosphosilicate- and arginine-containing desensitizing toothpastes for the random effects model was significantly different and the effect was flavoured, i.e., a large effect (less than −0.8 of overall SMD) of desensitizing toothpaste on dentin hypersensitivity, but not that of strontium-containing desensitizing toothpaste.

Potassium is the most popular ingredient for nerve desensitization. Potassium nitrate (5%), potassium chloride (3.75%) and potassium citrate (5.5%) are used, and all of them contain 2% of potassium ion and wield influence by interrupting the neural transmission for pain stimuli (Davies et al. 2010). Potassium salt increases extracellular potassium ion, passes the dentinal tubule, and depolarizes the nerve synapse to disrupt the conduction of pain impulse (Schiff et al. 1998). This meta-analysis indicates that potassium-containing toothpaste can ease the symptoms of dentin hypersensitivity, unlike the systemic review (Poulsen et al. 2006) conducted a decade ago, which questioned the effect of potassium-containing toothpaste because of failing to show a significant effect on the subjective assessment, despite the statistically significant effect on air blast and tactile sensitivity.

Stannous fluoride works by causing the chemical precipitation of insoluble metal compounds, blocking the opened dentinal tubule, and preventing the stimulation of free nerve ending as proven using scanning electron microscopy, electron probe microanalysis, and Vickers surface micro-hardness based on the deposition of tin and fluoride (White et al. 2007). It was concluded that stannous fluoride provides a desensitizing effect alone or when combined with potassium chloride.

Strontium chloride is the first ingredient used as desensitizer and has been used for 50 years by being combined with toothpaste; recently, strontium acetate, which can be combined with fluoride, has been used (Li et al. 2011). Strontium can be absorbed in the enamel and dentin due to the similar chemical and biological properties of calcium; strontium salt provides a desensitizing effect with layers of deposited small particles to block the dentinal tubule (Liu & Hu 2012). Nonetheless, it is controversial because the effect of strontium-containing toothpaste varies by study. The meta-analysis of five studies in this study suggested that strontium-containing toothpaste does not have a desensitizing effect.

**NovaMin** (GlaxoSmithKline Consumer Healthcare, Weybridge, Surrey, UK) is the trade name for inorganic, amorphous calcium sodium phosphosilicate. It is a bioactive material consisting of elements naturally occurring in the body chemistry and is part of the inorganic synthetic biomaterials known as bioactive glass-ceramics (Gendreau et al. 2011). It can be combined with dentin due to its high affinity with collagen, emitting calcium and phosphate when exposed to saliva,
an aqueous media. As a result, it provides an excellent desensitizing effect by creating protective hydroxyapatite – a component of teeth – and blocking the dentinal tubule (Gendreau et al. 2011). Arginine and calcium carbonate formulation is based on a naturally occurring biological process of tubule occlusion by salivary glycoproteins with calcium and phosphate (Shiau 2012). As an amino acid, Arginine is positively charged at physiological pH; bicarbonate acts as pH buffer to generate an alkaline condition that facilitates the accumulation of glycoprotein, whereas calcium carbonate serves as calcium source and naturally occludes the dentinal tubule (Cummins 2010); thus providing an excellent desensitizing effect.

The air blast test is a more accurate method of evaluating dentin hypersensitivity because it involves a wider area of dentin and it was also used more often than tactile test, thermal test, or subject assessment in clinical trials (Lin et al. 2013). In addition, it is physiological, controllable (Pradeep & Sharma 2010), and a more reproducible method for assessing dentin hypersensitivity (Ide et al. 2001) and is consequently used in many research studies. The diversity of methods of comparing the clinical effect on dentin hypersensitivity causes contradictory findings in test results; thus, the comparison of test results should be limited (Holland et al. 1997). Differences in the dentin hypersensitivity assessment methods could have led to discrepancies in the levels of reproducibility among studies, contributing to the high level of heterogeneity (Sgolastra et al. 2013). In this meta-analysis, we chose studies which used air blast test to minimize the heterogeneity of methods used.

Visual analogue scales (VAS), verbal rating scales (VRS), and the Schiff cold air sensitivity scale (SCASS) were used for evaluating the effects of desensitizing toothpaste in clinical trials. VAS consists of a straight line that is 10 cm long, the ends of which are defined with the words “no pain” and “severe pain.” The scale of VAS is usually 0–10 or 0–100 (Scott & Huskisson 1976). VRS use word descriptors as a scaling technique to describe the variation in pain. The VRS is usually 0–3: 0 for no discomfort; 1 for discomfort or mild pain; 2 for severe pain during stimulation, and; 3 for severe pain that persisted for some time after stimulation (Holland et al. 1997). The SCASS is usually 0–3: 0 for subject does not respond to air stimulus; 1 for subject responds to air stimulus but does not request discontinuation of stimulus; 2 for severe pain during stimulation, and; 3 for severe pain that persisted for some time after stimulation (Holland et al. 1997). The SCASS was usually 0–3: 0 for subject does not respond to air stimulus; 1 for subject responds to air stimulus but does not request discontinuation of stimulus; 2 for subject responds to air stimulus and requests discontinuation or moves from stimulus; 3 for subject responds to air stimulus, considers stimulus to

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<th>Table 2. Risk of bias and quality of the evidence of included studies</th>
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u, low risk of bias; u, unclear risk of bias; h, high risk of bias.
Fig. 2. Forest plot of the effect of desensitizing toothpaste on dentin hypersensitivity.
be painful, and requests discontinuation of the stimulus (Schiff et al. 1994). To combine data from different scales, we used SMD, which would be comparable across studies (Lin et al. 2013).

The follow-up period of included studies vary, depending on whether it was evaluating immediate effect or lasting effect of the product. The trial duration should be sufficient to allow expression of the active agent, while minimizing the magnitude of any placebo efficacy of the maximum effects (Holland et al. 1997). For instant relief effect evaluation, 3 days, 7 days, or 2 weeks timeframe was used, and for lasting relief effect evaluation, a 4-, 6-, 8-, or 12-week timeframe was used. While 8 weeks may be a suitable duration for most clinical trials, the optimum time course of product action should first be established in pilot studies (Holland et al. 1997). Clinical trial design should also recognize that the time required to achieve maximal desensitizing effects may vary between different products or agents (Collins & Perkins 1984).

All included studies sponsored by the manufacturers and high heterogeneity of the included studies were the main limitations of this study. There are limitations to this study and controversy with previous studies; therefore, further randomized trials that are well designed are needed to confirm these results.

In this study, most desensitizing toothpastes except the strontium-containing variant were effective, but the biggest weakness is the slow onset of the effect, i.e., a long time is required to see the desensitizing effect from the toothpaste. To overcome this weakness, the use of desensitizing toothpaste is recommended after experiencing an instant effect from in-office treatment to maintain and increase desensitizing effect. In addition, if the desensitizing toothpaste failed to remove the symptoms, visiting a dentist is recommended because it may be a dental caries or other disease.

Conclusion

The current meta-analysis of 31 randomized controlled clinical trials indicates that there is sufficient evidence to support the use of potassium-, stannous fluoride-, calcium sodium phosphosilicate-, and arginine-containing desensitizing toothpaste for dentin hypersensitivity, but not the use of strontium-containing desensitizing toothpaste, compared to placebo in adult dentin hypersensitivity sufferers.

Acknowledgements

J.H. Bae as principal investigator has full access to all of the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis. J.H. Bae and S.K. Myung were responsible for the study design, and statistical analysis. J.H. Bae and Y.K. Kim were responsible for data interpretation and manuscript drafting. The authors declare no conflicts of interest with respect to the authorship and/or publication of this article. No external funding was sourced for this study.

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Clinical Relevance

**Scientific rationale for the study:** A meta-analysis focusing on desensitizing toothpaste was performed to support dentist and patient information and decision making for choose desensitizing toothpaste.

**Principal findings:** Potassium-, stannous fluoride-, potassium and stannous fluoride-, calcium sodium phosphosilicate-, and arginine-containing desensitizing toothpastes reduce the symptoms of dentin hypersensitivity.

**Practical Implications:** This study would help dentists to recommend desensitizing toothpaste for dentin hypersensitivity patients, and give dentists and others useful information regarding the effects of desensitizing toothpaste on dentin hypersensitivity.