The Effect of Three Desensitizing Agents on Dentin Hypersensitivity: A Randomized, Split-mouth Clinical Trial

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Clinical Relevance
The desensitizing agents tested provided rapid and effective clinical relief of dentin hypersensitivity.

SUMMARY
The aim of this study was to evaluate the efficacy of three desensitizing agents to provide relief to dentin hypersensitivity after one session in a four-week follow-up. Forty selected patients participated in a double-blind study following a split-mouth model. One application of the desensitizing agents (A, Admira Protect [Voco]; B, Bifluorid 12 [Voco]; and C, Colgate Pro-Relief in office [Colgate Palmolive]) was performed in three different quadrants for each patient. Each tooth was evaluated by tactile and evaporative stimuli, and the sensitivity response was measured using the Visual Analogue Scale. Evaluations were performed at baseline, immediately after

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DOI: 10.2341/13-057
treatment, and after one, two, three, and four weeks. The application of Kruskal-Wallis and Dunn multiple comparisons tests (5%) for both tactile and evaporative stimuli showed that all agents presented a significant desensitizing effect. In groups A and B this relief was maintained for four and three weeks, respectively, as measured by tactile stimulus and for four weeks with evaporative stimulus. The desensitizing effect for group C was maintained for two weeks for both tactile and evaporative stimuli. It is concluded that all desensitizing agents tested were effective in reducing sensitivity compared to baseline values. One application of Admira Protect and Bifluorid 12 presented a longer-lasting desensitizing effect than did Colgate Pro-Relief (applied in the office) on both tactile and evaporative stimuli.

INTRODUCTION

Dentin hypersensitivity is characterized by short-term pain, intense and subtle, caused by thermal stimulus (such as that associated with water ingestion and hot or cold food) or by chemical (pH alteration) or mechanical (excessive pressure during tooth brushing and/or inappropriate brush use) actions in dentin areas exposed to the intraoral environment. This exposure can be a consequence of enamel loss through abrasion, abfraction, or erosion or it can result from root surface exposure caused by gingival recession, periodontal treatment, or the combination of both factors.

It was previously demonstrated that one in six people, both men and women, are affected by dentin hypersensitivity, with a greater incidence in elderly people. Other studies reported that the prevalence of dentin hypersensitivity in the population varies from 4% to 57%. This great variation is attributed mainly to the existence of various diagnosis methods and criteria of sample selection from the population. In addition, with the increase in the population’s life expectancy and the greater retention of elderly people’s teeth as a result of preventive care, a rise in cervical hypersensitivity may be expected.

The hydrodynamics theory proposed by Brännström in the 1960s is that most often accepted as an explanation for painful dentin transmission. According to this theory, when a stimulus is applied to the dentin, a flow movement occurs in the tubules. The dentin flow movement toward the pulp—or flow in the opposite direction—causes a mechanical deformation of the nerve fibers that are inside the tubule or of the dentin/pulp interface, which is transmitted as a painful sensation.

The desensitizing agents can be divided into groups based on their occlusive or neural action. The occlusive agents can work by different mechanisms, as the precipitation of proteins that are present in the fluid inside the tubule, precipitation of amorphous particles over the dentin and/or inside the tubule, or through mechanical action promoted by the formation of a superficial pellicle penetrating (or not penetrating) into the dentin tubules. The neural blocking method consists of the direct diffusion of potassium ions through the dental structure, raising its concentration in the pulp tissue and blocking the anoxic action (nerve impulse conduction) by the altering of its action potential.

Independent of the mechanism of action, the objective of hypersensitivity treatment is the immediate interruption of the pain.

The desensitizing agents can be applied by a professional (in-office treatment) or used by the patient at home. The great variety in both the treatment types and products for dentin sensitivity can be related to the fact that this problem is hard to treat or to the fact that there is not a desensitizing agent that is good enough to eliminate the patient’s discomfort. Therefore, the aim of the present study was to investigate the clinical efficacy of three different desensitizing agents in reducing dentin hypersensitivity over a four-week period. The null hypotheses tested were that 1) the desensitizing agents tested are not able to reduce the pain resulting from dentin hypersensitivity and 2) the desensitizing actions do not differ among the tested groups when tactile and evaporative stimuli are applied.

METHODS AND MATERIALS

The study protocol was approved by the local ethics committee.

Patient Selection

Forty patients who presented with some degree of sensitivity in at least three quadrants of the mouth were selected, yielding a total of 225 teeth. All patients received detailed information, both orally and in written form, and signed the appropriate informed consent forms outlining the purpose of the study.
The study inclusion criteria were that the patients had to be in good general health, be at least 18 years old, and have a minimum of one tooth that was sensitive in each of the three different quadrants of the mouth. The study excluded patients who were using desensitizing agents; were receiving periodontal treatment or had received nonsurgical periodontal treatment in the last three months; were receiving anti-inflammatory, psychotropic, or antidepressant drugs and analgesic medication; were pregnant or lactating; or had an allergy to any of the components in the treatment materials used in the study. In addition, patients with eating disorders and regurgitation or chronic diseases or who had received orthodontic treatment in the previous three months were also excluded. Also excluded were those with teeth having a painful condition involving the pulp and periapical region; those with any active caries or deep cervical lesions that required restoration; those with teeth having large restorations or who had been treated in the last three months; and those with abutment teeth for fixed and removable prostheses; as well as patients who had any fractured or cracked teeth.

**Evaluation of Sensitivity**

Two different operators worked in this study. One operator evaluated the response of each tooth to tactile and air stimuli for each patient and then measured and recorded the sensitivity. The second operator, who did not know the baseline sensitivity values for the teeth, applied the desensitizing agents to the teeth according to the manufacturers’ instructions. The researcher who applied the treatment had no access to the sensitivity scores, which provided for the double-blind nature of the study.

The teeth were cleaned with pumice and a rotary brush using a low-speed handpiece. For diagnosis, the quadrants were isolated with cotton rolls and the dental surface dried with cotton pellets. Then the teeth were subjected to mechanical and evaporative stimuli. For the mechanical test, a relatively constant mild force using manual pressure was applied in the mesiodistal direction across the cervical area of each tooth to determine the patient’s tactile response. Immediately after the stimulus, the operator requested that the patient score the pain using a Visual Analogue Scale (VAS) coupled with a Numeric Rating Scale (NRS).

The VAS/NRS scale used a plastic ruler 15 cm long, with a groove of 10 cm in the middle of its long axis and a button which the patient could move inside the groove from one extreme to the other. On each side of the ruler there was a different scale. On the side that was shown to the patient, corresponding to the VAS scale, “no pain” was written on the left extreme and “intolerable pain” written on the right extreme. After each stimulus, the patient moved the button to the position representing how much pain he/she was feeling. On the opposite side, not visible to the patient, there was a NRS scale, corresponding to the VAS but in numeric values. The NRS consisted of a span of 10 cm, with markings each 1 mm. After each patient marked on the VAS side the intensity of his sensitivity, moving the button to the appropriate position, the operator determined the sensitivity score by checking the number on the NRS side, corresponding to the mark determined by the patient on the VAS scale. The number corresponded to the distance (in centimeters) from the initial point (no pain) to the point the patient marked.

Five minutes after the mechanical test, the sensitive teeth were isolated from the adjacent teeth mesially and distally using cotton rolls in order to determine the response to the evaporative stimulus. A one-second blast of air from a dental unit syringe at 40-65 psi and a temperature of 19°C ± 5°C applied 1-3 mm away from and perpendicular to the exposed buccal cervical areas of exposed dentin was used, while adjacent teeth were protected with gloved fingers and cotton rolls to prevent false-positive results. The pain was recorded using the same VAS scale.

The sensitivity test was recorded by a calibrated examiner. Calibration procedures were performed using a dental mannequin, jet air/water, a stop-watch, and a dental explorer. The duration of the calibration process (training and calibration exercises) was approximately 20 hours. The order in which teeth were assessed in each patient was maintained at each visit. The examiner and the patient were blinded from the type of treatment performed in each quadrant. Each quadrant containing at least one sensitive tooth was randomly assigned to each of three treatments by lot. Each volunteer had at least one hypersensitive tooth in each quadrant. All sensitive teeth of each quadrant received the same treatment.

**Application of Desensitizing Agents**

For application of desensitizing agents, the teeth were cleaned with cotton pellets and dried with air. The operating field was isolated by means of cotton rolls and suction. Only one application of the products was carried out, according to the manufac-
turers' instructions (Table 1). The following desensitizing agents were applied: Admira Protect (Voco, Cuxhaven, Germany); Bifluorid 12 (Voco) and Colgate Sensitive Pro-Relief in office (Colgate Palmolive, Colgate-Palmolive Company, New York, NY, USA).

The present study used at least three quadrants, characterizing a “split-mouth” study. In each quadrant different desensitizing agents were randomly applied. The study did not include a “placebo” group for ethical reasons.

After application, the patients were instructed to avoid food and liquid intake for two hours and to avoid alcoholic beverages, brushing and flossing for 12 hours. The effectiveness of the products was tested immediately after desensitizer application with the VAS scale. The follow-up examinations using the same tactile and evaporative stimuli were performed after seven, 14, 21, and 28 days.

**Statistical Analysis**

The data were submitted to the nonparametric Kruskal-Wallis and Dunn multiple comparison tests. The significance level was set at 5%. The software program Statistix for Windows (version 8.0, Analytical Software, Tallahassee, FL, USA) was used for the calculations.

**RESULTS**

The percentage of variations of the subject responses for the treatment groups at baseline; immediately after treatment; and in the first, second, third, and fourth weeks are presented in Table 2. This table corresponds to differences in sensitivity values of each recall compared to baseline. The results obtained for negative values correspond to a reduction in pain sensitivity. The positive values account for an increased sensitivity value to painful stimuli. When differences in sensitivity values compared to the baseline did not occur, it was perceived to indicate no variation in pain. All desensitizing agents showed decreased levels of sensitivity following the revaluations after next recalls. In general, 50%-60% of the treated teeth continued showing reduced pain after four weeks for all agents.

The mean VAS scores for the treatment groups after receiving tactile and air stimuli are presented in Tables 3 and 4, respectively. The level of hypersensitivity to tactile stimulus for each desensitizer was compared among the different recalls using Kruskal-Wallis and Dunn tests (Table 3, columns). Significant differences were observed for all tested agents. For Admira Protect, an immediate and significant reduction was observed, and this difference was maintained throughout the additional four weeks of evaluation. Bifluorid 12 presented a significant desensitizing effect immediately after application, which was maintained for three weeks, although an increase in values was observed after four weeks. For Colgate Pro-Relief a significant desensitizer effect was noticed immediately, and reduced values were retained for two weeks. After
three weeks, the values were not significantly different from baseline.

In order to compare the performance among all desensitizers at each recall, Kruskal-Wallis and Dunn tests were applied (Table 3, rows). At the evaluation performed immediately after the application of the products, Admira Protect and Bifluorid showed a better performance than did Colgate Pro-Relief. However, in the further evaluations, the results were not significantly different.

The level of hypersensitivity to evaporative stimulus for each desensitizer separately was compared among the different recalls using Kruskal-Wallis and Dunn tests (Table 4, columns). For all desensitizers, significant differences were observed. For Admira Protect and Bifluorid 12, an immediate significant reduction was observed, and this difference was maintained during the four weeks of evaluation. For Colgate Pro-Relief a significant desensitizing effect was observed immediately and maintained for two weeks, although an increase was observed after three weeks.

### DISCUSSION

Pain sensation can be caused by different stimuli, such as chemical, mechanical or thermal stimuli, applied on exposed dentin under oral conditions. 

Several studies used a probe tip as a tactile stimulus because it causes the movement of the dentinal fluid as a result of the compression of the dentin. In addition to promoting the evaporation of the fluid inside the tubules, the air blast also decreases the temperature at the dentin surface. Both effects cause the movement of dentinal fluid from opened tubules. Using tactile and evaporative stimuli, the sensitivity level can be determined by VAS. This is considered the most appropriate method with which to diagnose pain levels because it allows for the

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**Table 2: Variations of the Subject Responses of the Treatment Groups Immediately After and at the First, Second, Third, and Fourth Weeks (in Percentage)**

<table>
<thead>
<tr>
<th>Variations of the VAS Scores</th>
<th>Evaporative, %</th>
<th>Tactile, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative Ranks&lt;sup&gt;a&lt;/sup&gt;</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>Positive Ranks&lt;sup&gt;b&lt;/sup&gt;</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>Ties&lt;sup&gt;c&lt;/sup&gt;</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td><strong>Immediately</strong></td>
<td>61</td>
<td>57</td>
</tr>
<tr>
<td><strong>1 wk</strong></td>
<td>57</td>
<td>52</td>
</tr>
<tr>
<td><strong>2 wk</strong></td>
<td>54</td>
<td>64</td>
</tr>
<tr>
<td><strong>3 wk</strong></td>
<td>55</td>
<td>56</td>
</tr>
<tr>
<td><strong>4 wk</strong></td>
<td>57</td>
<td>60</td>
</tr>
</tbody>
</table>

Abbreviation: VAS, Visual Analogue Score.

<sup>a</sup> Percentage of hypersensitivity reduction in relation to the baseline values for each product.

<sup>b</sup> Percentage of hypersensitivity growth in relation to the baseline values for each product.

<sup>c</sup> Percentage of maintenance hypersensitivity in relation to the baseline values for each product: A) Admira, B) Bifluorid 12, and C) Colgate ProRelief.

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**Table 3: Mean Visual Analogue Scores (VASs) and Percentage of Hypersensitivity Reduction for the Treatment Groups After Receiving Tactile Stimuli over Four Weeks**

<table>
<thead>
<tr>
<th>Recalls</th>
<th>Admira Protect Mean ± SD&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Bifluorid 12 Mean ± SD&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Colgate Pro-Relief Mean ± SD&lt;sup&gt;a&lt;/sup&gt;</th>
<th>K-W&lt;sup&gt;d&lt;/sup&gt; (df=2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>3.59 ± 3.08 aA</td>
<td>3.63 ± 3.07 aA</td>
<td>3.35 ± 3.11 aA</td>
<td>p = 0.787, H&lt;sup&gt;d&lt;/sup&gt; = 0.47</td>
</tr>
<tr>
<td>Immediately</td>
<td>0.93 ± 1.85 bA</td>
<td>1.67 ± 2.31 bAB</td>
<td>1.92 ± 2.88 bB</td>
<td>p = 0.014, H = 8.46</td>
</tr>
<tr>
<td>1 wk</td>
<td>1.54 ± 2.27 bA</td>
<td>1.82 ± 2.29 bAB</td>
<td>1.65 ± 2.43 bA</td>
<td>p = 0.344, H = 2.12</td>
</tr>
<tr>
<td>2 wk</td>
<td>1.82 ± 2.45 bA</td>
<td>1.82 ± 2.46 bA</td>
<td>1.86 ± 2.46 bA</td>
<td>p = 0.985, H = 0.02</td>
</tr>
<tr>
<td>3 wk</td>
<td>2.04 ± 2.76 bA</td>
<td>2.05 ± 2.60 bA</td>
<td>1.97 ± 2.70 abA</td>
<td>p = 0.864, H = 0.29</td>
</tr>
<tr>
<td>4 wk</td>
<td>1.84 ± 2.52 bA</td>
<td>2.27 ± 2.60 abA</td>
<td>2.06 ± 2.80 abA</td>
<td>p = 0.255, H = 2.72</td>
</tr>
<tr>
<td>K-W&lt;sup&gt;f&lt;/sup&gt; (df=5)</td>
<td>p = 0.000&lt;sup&gt;c&lt;/sup&gt;</td>
<td>p = 0.000&lt;sup&gt;c&lt;/sup&gt;</td>
<td>p = 0.002&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Results of Kruskal-Wallis test for the comparison among the desensitizers for the same recall.

<sup>b</sup> Different lowercase letters in columns indicate significant differences among each recall for the same desensitizer, while different capital letters in rows indicate significant differences among the desensitizers for the same recall.

<sup>c</sup> Results of Kruskal-Wallis test for the comparison among the different recalls for the same desensitizer.

<sup>d</sup> Kruskal-Wallis H statistic.
translation of the subjective feedback into objective data.29

In the present study, the first null hypothesis was rejected, since the three agents tested showed efficacy in reducing sensitivity, even with a single application. The reduction of pain sensitivity was in general greater than 50% (52%-60% and 54%-57% evaporative and tactile stimuli, respectively).

The second null hypothesis tested was also rejected when tactile stimulus was applied, as the patients reported significantly higher sensitivity relief immediately after the application of Admira Protect, compared to Colgate Sensitive Pro-Relief. For the evaporative stimulus, there were no significant differences among the tested groups. Indeed, it was previously reported that the type of stimulus can influence the painful response.29,33,34 The tactile stimulus was applied prior to the evaporative since the use of air blast results in irreversible dehydration of dentin. Although the interval between stimulus applications should be of sufficient duration to minimize interactions between stimuli, the appropriate interval is not known.35 Thus, it was expected that a five-minute interval between the application of evaporative and tactile stimuli would be appropriate, according to previous studies.27,28

Colgate Sensitive Pro-Relief consists of arginine, a positively charged amino acid, in physiological pH, with bicarbonate as a pH buffer and calcium carbonate. This kind of agent was developed in an attempt to seal patent dentinal tubules and, consequently, to relieve hypersensitivity. Its action is based on the natural role of saliva, which contains arginine and calcium carbonate and provides calcium and phosphorus ions to migrate to patent tubules and create a precipitate of salivary glycoproteins and calcium phosphate, occluding the tubules. Studies23,36 have shown that the plug composed of arginine, calcium carbonate, and phosphate within dentin tubules effectively reduced the fluid dentinal flow and, consequently, minimized sensitivity. Previous clinical data37,38 also demonstrated the effectiveness of this product in reducing sensitivity. In the present study, the single application of the professional desensitizing paste Colgate Sensitive Pro-Relief, simulating an in-office application, resulted in an immediate reduction of sensitivity, but at the third-week assessment, the values increased and were not significantly different from the baseline values.

The application time may interfere with the efficacy of this agent. A scanning electron microscopy (SEM) analysis36 of exposed dentin tubules treated with Colgate Sensitive Pro-Relief for 30 seconds showed a partial tubule lumen obliteration, with reduction of the dentin permeability (69.8%). On the other hand, when the application time was increased to one minute, the tubule obliteration was complete.39 Nevertheless, Petrou and others39 stated that even though the tubules were obliterated, the fluid movement inside the dentin tubules was not completely inhibited; hence, the pain may persist.39 Thus, it should be necessary to undergo multiple applications in seeking a longer-lasting protective coating. Therefore, the in-office use should be associated with the at-home toothpaste.

Various fluoride-based products have been tested as desensitizing agents, with different formulations, such as sodium fluoride, stannous fluoride, sodium monofluorophosphate, and fluorosilicate.22 Fluoride
can be added in varnishes, since they are common agents used as a dentin sensitivity treatment, providing a barrier that seals the exposed dentin. The fast-drying varnish that adheres to the surface makes it possible to achieve long-term intensive fluoridation, retaining the fluoride as long as possible on the surface so that the fluoride is able to act. However, although the varnish can produce an immediate desensitizing effect, it has been stated that these materials exhibit low adhesion that is easily removed by saliva or by the abrasion caused by brushing. The fluoride varnish Bifluorid 12 is composed of 6% calcium fluoride and 6% sodium fluoride. It creates a barrier by precipitating calcium fluoride on the dentin surface and causes the occlusion of the dentin tubules.

In the present study, the application of Bifluorid 12 reduced dentin hypersensitivity. According to the manufacturers, the sodium fluoride dissociates, releasing F⁻ ions, which diffuse into the tubules and are precipitated as calcium fluoride as a result of the high calcium concentration in dentinal fluid and saliva. The calcium fluoride present in the varnish composition diffuses into the tubules and seals the canal with a semipermanent protective layer. Therefore, the calcium fluoride present in Bifluorid 12 is added to close the dentin tubules mechanically, in combination with the calcium fluoride buildup by the sodium fluoride reaction to the calcium of dentin. Previous authors reported the effectiveness of this product in reducing sensitivity during a one-month assessment study and found some degree of sensitivity reduction even after 12 months. The tubule occlusion was demonstrated immediately after the application of Bifluorid 12 using SEM. However, after one month, some tubules had reopened. This may be due to the low bonding of varnish to dentin, since it can be peeled off of the dentin surface, reducing its mechanical desensitizing effect, and this may be the reason for the reduction of relief effect after three weeks when tactile stimulus was applied in this group. According to the manufacturers, for a more durable effect the application should be repeated two or three times at intervals of seven days. Nevertheless, in the present study, one single application was effective to relieve sensitivity for four weeks in most of the cases.

Admira Protect is a desensitizer that is based on bisphenol A diglycidyl ether dimethacrylate and 2-hydroxyethyl methacrylate monomers, organic acids, and ormocer. Ormocer materials contain inorganic-organic copolymers and inorganic silanated filler particles. According to the manufacturers, this material acts in a manner similar to that of a self-etching adhesive. It bonds to the dentin and penetrates into the tubules, creating resinous tags and a polymer layer over the surface. It is able to seal the dentin surface, reducing fluid flow. In contrast to fluoride varnish, the tubules are sealed with a light-curing material.

In the present study, Admira Protect exhibited the best performance relative to hypersensitivity reduction detected by tactile stimulus when the evaluation was performed immediately after application. A previous SEM investigation showed the efficacy of this agent in the obliteration of the dentinal tubules. Moreover, its desensitizing effect was maintained during the four-week evaluation. This longer-lasting effect may be related to the product’s components. The resinous monomers are able to adhere to dentin, forming a hybrid layer. In addition, Admira Protect contains fillers, which may promote higher resistance to abrasion, avoiding the removal of the product layer by tooth brushing.

Clinically, several treatments and products to reduce the dentin hypersensitivity have been tested. All desensitizing agents tested in the present study reduced the dentin sensitivity after one application during the four-week evaluation. However, the efficacy of the products varied among the studies and the methodologies employed. Thus, the results from different clinical trials must be considered with caution, since the dentin hypersensitivity analysis involves subjective aspects.

CONCLUSION

Based on the methodology used, it can be concluded that

- All desensitizing agents tested were efficient in reducing hypersensitivity. They were equally effective when tactile and evaporative stimuli were applied at each recall, although Admira Protect presented a significantly better immediate effect with tactile stimulus.
- Admira Protect and Bifluorid 12 showed a longer-lasting desensitizing effect in relation to Colgate Pro-Relief on both tactile and evaporative stimuli after one application.

Conflict of Interest

The authors of this manuscript certify that they have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.
REFERENCES


