The Clinical Effect of Amorphous Calcium Phosphate (ACP) on Root Surface Hypersensitivity

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Clinical Relevance
Sequential applications of solutions that form amorphous calcium phosphates are effective for rapidly decreasing dentin hypersensitivity.

SUMMARY
Dentin hypersensitivity is a transient condition that often resolves with the natural sclerotic obturation of dentin tubules. A method of rapidly forming calcium phosphate compounds within these tubules can mimic sclerosis and lead to rapid reduction in hypersensitivity. Amorphous calcium phosphates (ACP) can be formed in situ by the sequential application of calcium and phosphate solutions. In this clinical study, 30 patients with reported dentin hypersensitivity were randomly assigned to parallel treatment or placebo groups. In the experimental treatment group, ACP was formed by topical application of a 1.5 mol/L aqueous solution of CaCl₂ followed by topical application of 1.0 mol/L aqueous K₃PO₄. The placebo group was treated with a topical application of 1.0 mol/L aqueous solution of KCl followed by topical application of distilled water. Treatments were repeated at the 7-day and 28-day recall appointments. Response to air and tactile stimuli were measured immediately before treatment using a visual analog scale initially on day 1, then on days 7, 28 and 180. The results showed that both the experimental and placebo treatments resulted in a reduction in hypersensitivity at 180 days. However, the ACP treatment
group showed a much more rapid reduction in hypersensitivity over time. The change in sensitivity was much more apparent using the air stimulus than the tactile stimulus. These results show that topical placement of ACP can rapidly reduce dentin hypersensitivity.

INTRODUCTION

The clinical condition of dentin hypersensitivity is a significant problem in the adult population. Gingival recessions, root surface debridement or periodontal surgical procedures often cause the exposure of orifices of the dentin tubules at the root surface. The origin of dentin sensitivity has been described (Brännström, Linden & Åström, 1967; Paschley, 1990) as being due to mechanical, osmotic or thermal stimuli that can communicate with pulpal sensory nerves through these open tubules. The current approach to treating this condition is to obturate the dentinal tubules using a variety of agents, such as fluoride varnishes (Lukomsky, 1941; Lutins, Greco & McFall, 1984), Oxalate salts (Paschley & Galloway, 1985), and resinous agents (Paschley, & others, 1988; Trowbridge & Silver, 1990). The treatments mentioned above generally result in only partial or short-term relief of the dentin hypersensitivity (Morris, Davis & Richardson, 1999). Many treatments are not compatible with ongoing dental treatment, such as periodontal flap surgery.

Calcium phosphate minerals are the main inorganic constituents of dentin, and mineral rich deposits obstruct tubule orifices in the physiological process of dentin sclerosis (Frank, 1968). A method of mimicking this natural process may provide an effective clinical treatment for dentin hypersensitivity. Of the available calcium phosphate compounds, amorphous calcium phosphate (ACP) has the highest rate of formation and dissolution under physiological oral conditions. This compound is also capable of rapid conversion into hydroxyapatite crystals under these same conditions, which can precipitate in the lumen of open dentinal tubules (Tung & others, 1992; Tung & others, 1993; Tung, O’Farrell & Liu, 1993). Previous research by Tung and others (1997) established the concentrations and mode of application for clinically applying ACP as a topical desensitizer, and preliminary clinical investigations indicated that this might provide an efficient treatment for dentin hypersensitivity. This study clinically assessed the effect of topical application of ACP forming calcium phosphate solutions or dentin hypersensitivity.

METHODS AND MATERIALS

Thirty adult patients exhibiting clinical symptoms of dentin hypersensitivity participated in this study. The clinical history of all the candidates was documented, and those suffering any illness or allergies or those receiving any kind of medication were excluded. Subjects participating in the study presented a minimum of two sensitive teeth in a minimum of two different quadrants. All subjects exhibited good dental care and had their last oral hygiene treatment within the last six months. Patients were randomly assigned to a treatment or a control group in a parallel design. This design was chosen to prevent crossover from the experimental treatment to the control teeth. No hazards or deleterious side effects were observed in previous studies of this material and none were anticipated in this study. The Helsinki Committee of Tel-Aviv University approved the study. Each subject signed a consent form after a full explanation of the treatment procedure and the known risks and effects.

Materials

Amorphous Calcium Phosphate is precipitated under oral physiological conditions by the sequential application of calcium chloride solution followed by a potassium phosphate solution (Tung & others, 1993). For the experimental group patients, two solutions were sequentially applied to the root surface: Solution A containing an aqueous solution of 1.5 mol/L calcium chloride, and Solution B containing an aqueous solution of 1.0 mol/L tripotassium phosphate. In the control group, a placebo material composed of two solutions was also sequentially applied: Solution PA containing 1.5 mol/L KCl, and Solution PB containing distilled water. For both the experimental and control treatments, the two solutions were applied successively over the root surfaces of each quadrant using a cotton pellet saturated with the solution and rubbing the material on the sensitive tooth surface for five seconds. Cotton rolls were used to isolate the treatment area. After rubbing, the solutions stayed undisturbed on the tooth surface for 60 seconds. The patients were then asked not to rinse, eat or drink for 30 minutes after treatment. The treatment was repeated at 7- and 28-day recalls, for a total of three treatments. Both the ACP and placebo solutions were coded and were unknown to the patient or the examiner during the experiment.

Sensitivity Test

The level of sensitivity was evaluated at the initial visit and at recalls after one week (seven days), four weeks (28 days) and six months (180 days). At the 7- and 28-day recalls, sensitivity measurements were made prior to re-treatment. No treatment was delivered at the 180-day recall. The patient was asked to define the degree of sensitivity using a visual analog scale by placing a vertical mark on a 100 mm line where 0 was "no pain" and 100 was "severe pain." The location of the mark was measured in mm from the line of origin and the results were coded and recorded for further statistical analysis. Tactile sensitivity was evaluated by measuring the response to the contact of an explorer over the cervical area of each tooth. Air sensitivity was exam-
inced using the dental unit triple syringe and blowing a short blast of room temperature air over each root surface. Each tooth was isolated during measurement by placing cotton rolls over the adjacent teeth.

**Statistical Analysis**

The results were analyzed using two-way Analysis of Variance (ANOVA) with repeated measures of time and treatment as primary variables. The significance level used was $\leq 0.05$ one tailed. Standard Deviations (SD) were calculated for all analyses. The statistical analysis was performed using the SPSS program.

**RESULTS**

Chi-square analyses were conducted to determine whether significant correlations could be found between treatments and such factors as gender; periodontal condition, rated as healthy, mild inflammation or severe inflammation; quality of oral hygiene rated as good, fair or poor; toothbrush type rated as soft, medium and hard; whether a mouthwash was used; whether previous periodontal surgery was done; whether a six month recall had been completed; and whether they were smokers. No significant correlations were found, indicating that the patients were fairly balanced over the study groups.

Applying ACP to the root surfaces resulted in a rapid decrease in air sensitivity. Within seven days after treatment, air sensitivity was reduced from the initial mean value of 43.2 to a mean value of 31.4. Examination of these same patients three weeks later revealed a further decrease in sensitivity, reaching values of 26.3 and remaining at about the same level at the fourth examination after 180 days (Figure 1). The control treatment, where no significant change was noted from 50.4 to 49.7 after seven days, to 48.1 after 28 days and to 41.3 after 180 days (Figure 1), was also noted. The Analysis of Variance on the transformed data for air response showed that time was a significant factor ($p<0.004$) with sensitivity score dropping over time. Treatment was also significant ($p=0.041$), but no significant interaction was present between time and treatment ($p=0.230$).

Examination of tactile sensitivity (Figure 2) revealed a slower reduction in sensitivity after applying ACP from 25.7 to 22.6 after seven days, to 10.9 after 28 days, with no additional reduction (10.4) after 180 days. The control group showed a nearly parallel reduction, but with a higher sensitivity starting value at the initial measurement (Figure 2). The Analysis of Variance for tactile sensitivity showed, again, that time was a significant factor ($p<0.001$), with sensitivity being reduced with time. Treatment method was also significant ($p=0.041$), and there was no significant interaction between time and treatment ($p=0.984$).

**DISCUSSION**

Dentin hypersensitivity is a clinical situation characterized by a short, sharp pain initiated by many types of stimulation, such as tactile, thermal, osmotic or chemical (Pashley, 1990). According to the hydrodynamic theory of Bränström, Linden and Aström (1967), these stimulations, applied at the exposed dentin surface, cause an inward pressure on the tubular fluid, exciting the nerve endings within the pulp. Most current strategies for treating dentin hypersensitivity are by occlusion of tubular orifices at the tooth surface. In order to create an efficient, long lasting seal,
the material used to occlude this orifice should penetrate the tubule, be chemically stable and adhere to the intratubular dentin. Combe and Douglas (1998) proposed that developing a biomimetic material that is structurally similar to the dental hard tissue could possibly provide a solution for treating dentin hypersensitivity. Tung and others (1997) has postulated that since calcium phosphate is the main inorganic component of the tooth, calcium phosphate minerals are ideal candidates for the obstruction of dentinal tubules. Tung and others (1992) have also shown that calcium phosphate solutions at high concentrations and at pH=9.5 rapidly precipitate amorphous calcium phosphate that obstructs dentinal tubules and decreases dentin permeability by 85% or more.

In this study, the effectiveness of ACP was evaluated clinically as a possible therapeutic agent for the treatment of dentin hypersensitivity. The results demonstrated an immediate relief of sensitivity tactile and air stimulation after topical application of ACP. The alleviation was noted after 7 and 28 days, with further reduction in sensitivity after each repeated treatment. Beyond 28 days, the effect leveled off, and at 180 days, the difference between ACP and the placebo treatment was less notable. A possible explanation for this phenomenon might be that a spontaneous reduction in sensitivity occurs, probably due to minerals from salivary origin obstructing the tubular orifices. Alleviating sensitivity to air stimulation was more striking than alleviating sensitivity to tactile stimulation. A possible hypothesis that might explain this phenomenon is that mineral plugs of calcium phosphate that obstruct the tubular orifices at the dentin surface are not stable at the initial phase. Immediate contact of the explorer at the surface causes a pressure that is exerted on the tubular fluid, stimulating nerve endings at the pulp and causing the pain sensation. It is also difficult to precisely stimulate the same area of the tooth from one examination to another, leading to greater variation in results and the inability to discern differences in treatments. Tung and others (1997) also reported greater variability in tactile response in a prior clinical study.

The results of this study indicate that ACP may be used clinically for the fast relief of dentin hypersensitivity. The mode of application was found to be easy, and may be feasible even for auxiliary staff. No prior surface conditioning was used other than normal brushing and flossing. The solutions were easily placed using cotton tip applicators and isolation with cotton rolls was maintained during treatment. The precipitation of calcium phosphates provides a very natural and biocompatible treatment that does not require surface conditioning or the application of resins or polymers. This may make the treatment much more compatible with periodontal procedures such as deep scaling and root planing or surgical flap procedures.

CONCLUSIONS

The results of this clinical study showed that sequential application of calcium and phosphate-containing solutions that can form amorphous calcium phosphate in situ will more rapidly and more effectively reduce dentin hypersensitivity than a placebo treatment.

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