Effect of two desensitizing agents on dentin hypersensitivity: A randomized split-mouth clinical trial

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Abstract

Background: Clinical research is important to evaluate the effect of desensitizing agents.

Aims: This randomized clinical trial evaluated the immediate and 1 week desensitizing effect of two desensitizing agents Uno Topical Gel and Profluorid.

Materials and Methods: Thirtyfive patients with teeth presenting with dentin hypersensitivity were included in this clinical trial. Each quadrant in a patient was randomly assigned to one of two groups: Uno Topical Gel or Profluorid Varnish. A VAS score was used to assess tooth sensitivity at baseline, immediately after application of desensitizer and after 1 week. Additionally, 30 dentin discs were prepared, divided into Group 1(Control Group), Group 2 (Profluorid Varnish) and Group 3 (Uno Topical Gel) and examined using scanning electron microscopy (SEM) after 1 hour and 24 hours to evaluate tubule occlusion.

Statistical Analysis: Clinical data were analysed using Friedman’s test and Mann – Whitney U test. SEM data was analysed using Student’s 2-sample t-test.

Results: Uno group was significantly better to evaporative stimuli immediately (P=0.01) after application. After 1 week, Uno group was significantly better to tactile (P=0.000) and evaporative (P=0.000) stimuli than Profluorid. SEM images showed that 1 hour after application, Uno and Profluorid demonstrated more than 90% and 80% dentin tubule occlusion respectively. At 24 hours, Uno and Profluorid demonstrated more than 50% and 60% dentin tubule occlusion respectively.

Conclusions: Uno Topical Gel was significantly better than Profluorid in reducing pain of dentin hypersensitivity due to tactile and evaporative stimuli after 1 week.

Keywords: Dentin hypersensitivity; desensitizing agents; randomized clinical trial; scanning electron microscopy

INTRODUCTION

Dentin hypersensitivity is an exaggerated response to sensory stimuli. It can affect eating, drinking, and sometimes breathing. Increased dentin hypersensitivity can hinder effective plaque control, which can compromise oral health.[11] Dentin hypersensitivity can be due to dentin exposure resulting from the loss of enamel by tooth wear during abrasion and erosion, or by root surface denudation as a result of the gingival recession or periodontal treatment.[12] It can result in pain in one or more teeth due to either a thermal, chemical, mechanical, or osmotic stimuli.[13] Patients may variously

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describe symptoms as sharp or dull and which may be intermittent or constant, and it has been reported that 10%–30% of the general population may suffer from dentin hypersensitivity.\cite{4} Similarly, a recently published systematic review and meta-analysis concluded that the average prevalence of dentin hypersensitivity was 33.5%.\cite{5} Dentin hypersensitivity was found to be more common in the age group of 30–49 years with maxillary premolar and molar teeth being mostly affected while the most common initiating factor was cold liquids.\cite{6}

Dentin hypersensitivity is caused by the stimulation of exposed dentin and is mainly explained by the hydrodynamic theory proposed by Brannstrom. According to this theory, dentin stimulation results in the flow of fluid in the dentinal tubules, which may be transmitted to nerve fibers at the dentin/pulp interface.\cite{7} Therefore, occlusion of exposed dentinal tubules may be an important factor in the treatment of dentin hypersensitivity.\cite{8} The occlusive agents can reduce dentin permeability by different physicochemical mechanisms such as the growth of intratubular crystals or adsorption of plasma proteins within dentinal tubules.\cite{9} Dentin desensitization can also result from agents that can cause nerve desensitization.\cite{10} The neural blocking method can be due to direct diffusion of potassium ions through the dentin, increasing its concentration in inner dentin, which can result in nerve inactivation.\cite{11}

Dentin hypersensitivity can be treated by various in-office treatment options or by application of desensitizing agents by the patient at home.\cite{12} However, there is a great variety in the types of treatment and desensitizing agents available, and there is insufficient data concerning the relative effectiveness of these treatments.\cite{13} Furthermore, there is no consensus regarding a gold standard in the treatment of dentin hypersensitivity.\cite{14} Dentin hypersensitivity has been conventionally treated with fluoride.\cite{4} However, newer bio-active polymers have been developed which do not contain fluorides and are currently available to treat dentin hypersensitivity.\cite{15} Therefore, the aim of this study was to investigate dentin tubule occlusion of two different desensitizing agents, i.e., Profluorid Varnish (Voco, Cuxhaven, Germany) containing 5% sodium fluoride and Uno Topical Gel (Germiphene, Brantford, Canada) containing bio-active polymers on reducing dentin hypersensitivity. Next, the clinical efficacy of both desensitizing agents was evaluated by application of tactile and evaporative stimuli, since both such stimuli can provoke dentin hypersensitivity on exposed dentin.\cite{3} Thus, the null hypotheses tested in our study were: (1) the desensitizing agents evaluated are not able to reduce the pain resulting from dentin hypersensitivity and (2) the extent of desensitization does not differ between the tested agents when tactile and evaporative stimuli are applied.

METHODS

Evaluation of dentin tubule occlusion

Ethical committee approval was obtained from the University Review Board of Thai Moongambigai Dental College and Hospital, Dr. MGR Educational and Research Institute. This study was registered in the national clinical trials registry (CTRI/2019/05/019252).

Preparation of dentin discs

Thirty human unerupted, surgically extracted third molars were collected and stored in a 0.9% saline solution. They were sectioned parallel to the occlusal plane, starting below the occlusal surface in sections of 1.5 mm. The first disc above the pulp chamber was selected from each tooth. The discs were sonicated in a water bath for 10 min to remove debris. Next, they were treated with 17% ethylenediaminetetraacetic acid for 5 min to remove the smear layer and rinsed with distilled water.

The dentin discs were randomly divided into three groups of 10 samples in each and incubated in artificial saliva for 1 h before treatment. Artificial saliva was prepared based on a formulation used in oral drug release studies.\cite{16} Dentin discs were treated as follows: Group 1 (n = 10): No treatment (Control Group), Group 2 (n = 10): Treated with Profluorid Varnish and Group 3 (n = 10): Treated with Uno Topical Gel.

The dentin discs’ surface was gently air-dried. Profluorid Varnish and Uno Topical Gel were applied by a micro brush according to the manufacturer’s instructions. The dentin discs were incubated in artificial saliva for time points of 1 h (n = 5) and 24 h (n = 5) for each group. At the end of each time interval, the discs were rinsed in distilled water before being dried in preparation for scanning electron microscopy (SEM).

The dentin occlusion was analyzed quantitatively. Each image was analyzed for the total number of tubules, the number of open tubules, partially occluded tubules and completely occluded tubules. The percentage of partially and completely occluded tubules was calculated per image and averaged for the total number of images. The images were assessed to score the level of tubule occlusion on a categorical scale of 1–5, in accordance with the tubule occlusion classification scoring system, where: Score 1: Completely occluded tubules (100% of tubules occluded); Score 2: Predominantly occluded tubules (50% <100% of tubules occluded); Score 3: Partially occluded tubules (25% <50% occluded); Score 4: Mostly unoccluded tubules (<25% of tubules occluded); and Score 5: Unoccluded tubules (0%, no tubule occlusion). The mean score of the tubule occlusion was plotted in the graph.\cite{17}
Pradeepkumar, et al.: Effect of desensitizing agents on dentin hypersensitivity

When

In each

Images

Immediately, the patient was requested to score Numeric values to a span from left extreme to the right extreme. After each stimulus, the pain using a VAS. The VAS used a plastic ruler with "no pressure in mesiodistal direction across the cervical area was applied, and VAS score was again recorded using the same scale. When hypersensitivity evaluation was done for more than one tooth in a quadrant, the mean VAS score was calculated as the score for that quadrant.

Randomized split-mouth clinical trial

Preoperative evaluation

Fifty patients who presented with a complaint of dentin hypersensitivity to the Department of Conservative Dentistry were considered for the study, which was conducted in July 2019. Patients who were receiving or had received periodontal treatment within the past 3 months; used desensitizing treatment within the past 6 months; using anti-inflammatory, analgesic, psychotropic, or anti-depressant drugs: were pregnant or lactating; were allergic to any of the components in the desensitizing agents used in the study; and patients with eating disorders were excluded. In addition, teeth with carious lesions, cracked/fractured teeth, or teeth that required restorative management were excluded. A pilot study was done on ten patients, and sample size calculation (n = 30) was done based on the results obtained. The sample size was calculated using G power v. 3.1.9.2 based on the proportional difference formula with an alpha-type error of 0.05 and a power-beta of 0.95. The estimated sample size was 30 teeth per group. Thirty-five patients with good general health, within 18–60 years of age, with dentin hypersensitivity in at least one tooth in any two quadrants and exhibiting pain scores of two or more on the visual analog scale (VAS) were included in the study. The patients were well informed about the procedure, both orally and in a written form. Appropriate informed consent was obtained.

Evaluation of dentin hypersensitivity

The teeth were cleaned with pumice and rotary brush using a slow speed handpiece and isolated with cotton pellets and suction. The tactile stimulus was applied with an explorer with a constant mild force and manual pressure in mesiodistal direction across the cervical area. Immediately, the patient was requested to score the pain using a VAS. The VAS used a plastic ruler with “no pain” written on the left extreme and “intolerable pain” written on the right extreme. Numeric values to a span of 10 cm with markings after each 1 mm also extended from left extreme to the right extreme. After each stimulus, the patient was shown the VAS scale and requested to indicate the intensity of sensitivity he/she was feeling from number 1, indicating “no pain” to number 10, indicating “intolerable pain.”

A placebo group was not used for ethical reasons. The study deployed two different operators: one operator recorded sensitivity scores for the teeth after evaporative and tactile stimuli using VAS system. The second operator who was not aware of the sensitivity scores applied the designated desensitizing agent providing for the double-blind nature of the study. The patients were instructed to avoid eating/drinking for 2 h and avoid brushing for 12 h. Hypersensitivity assessment was done immediately after the application of desensitizing agents and after 1 week using the same tactile and evaporative stimuli. Further, dentin tubule occlusion after application of Profluorid Varnish (Voco, Cuxhaven, Germany) and Uno Topical Gel (Germiphene, Brantford, Canada) was evaluated.

Statistical analysis

Statistical analysis of the data was performed using the Statistical Package for the Social Sciences, IBM Corporation, SPSS Inc., Chicago, IL, USA version 21.0. The mean value of tubule occlusion was analyzed using the Student’s 2-sample t-test. Descriptive statistics, including mean, mean rank, and standard deviation, were computed. Normality analysis using Shapiro–Wilk test revealed that the data does not follow a normal distribution. Therefore, the determination of statistical significance was done using nonparametric tests. The differences within the group after baseline and different timeframes were assessed using Friedman’s test. Differences between the groups were analyzed using the Mann–Whitney U test. A value of $P < 0.05$ was considered statistically significant.
RESULTS

Dentin tubule occlusion
Dentin tubule occlusion was demonstrated at 1 h and 24 h after both Uno and Profluorid applications. 1 h after application, both Uno and Profluorid demonstrated >90% ($P < 0.001$) and 80% ($P < 0.001$) dentin tubule occlusion, respectively, with an average score of 1 for tubule occlusion [Figure 2a and b]. At the 24 h mark, Uno demonstrated >50% dentin tubule occlusion ($P < 0.001$) [Figure 2c], while Profluorid demonstrated >60% dentin tubule occlusion ($P < 0.001$) [Figure 2d] as compared to controls.

Clinical trial
Five patients were lost to follow-up, and data from 30 patients were analyzed. Within the Uno group, the mean pre-operative VAS scores after receiving tactile stimuli [Table 1] were $2.47 \pm 0.86$. After the immediate application of desensitizing agent, it significantly reduced to $0.00 \pm 0.00$ ($P = 0.000$). The mean VAS scores were reduced to $0.7 \pm 0.36$ at 1-week examination, which was found to be statistically significant ($P = 0.000$). There was 100% reduction immediately after the application of the agent. The overall reduction of sensitivity after 1 week was 72% for the UNO group.

In the profluorid group, the mean pre-operative VAS scores after receiving tactile stimuli [Table 1] were $2.67 \pm 0.95$. After immediate application of desensitizing agent, it reduced to $0.00 \pm 0.00$ ($P = 0.000$). The mean VAS scores were reduced to $2.0 \pm 0.00$ at 1-week examination, which
was found to be statistically significant ($P$ = 0.000). There was 100% reduction immediately after the application of the agent. The overall reduction of sensitivity after 1 week was 25% for the profluorid group.

In the Uno group, the mean pre-operative VAS scores after receiving evaporative stimuli [Table 2] were 4.4 ± 0.814. After the immediate application of a desensitizing agent, it reduced to 0.40 ± 0.00 ($P$ = 0.000). The mean VAS scores were reduced to 0.60 ± 0.932 at 1-week examination, which was found to be statistically significant ($P$ = 0.000). There was 91% reduction immediately after the application of the agent. The overall reduction of sensitivity after 1 week was 86% for the Uno group.

Table 2: Mean visual analog scale scores for the two treatment groups after receiving evaporative stimuli over different time intervals

| Treatment groups | n | Mean±SD | Mean rank | P     |
|------------------|---|----------|-----------|-------|
| UNO              |   | 4.4±0.814 | 3.00      | 0.000*|
| Pre-operative    | 30| 0.00±0.00  | 1.48      | 0.000*|
| Immediate        | 30| 0.07±0.36  | 1.52      |       |
| Profluorid       |   | 2.67±0.95  | 2.67      | 0.000*|
| Pre-operative    | 30| 0.00±0.00  | 1.00      |       |
| Immediate        | 30| 2.00±0.00  | 2.33      | 2.33  |

*Highly significant. Mann-Whitney U-test. SD: Standard deviation

In the profluorid group, the mean VAS scores after receiving evaporative stimuli [Table 2] were 4.4 ± 0.814. After the immediate application of desensitizing agents, it reduced to 0.40 ± 0.00 ($P$ = 0.000). Examination after 1 week showed an increase in mean VAS score to be 2.0 ± 0.00. These differences were found to be statistically highly significant. There was 91% reduction immediately after the application of the agent. The overall reduction of sensitivity after 1 week was 55% for the profluorid group.

There was no difference between the Uno group and Profluorid group in preoperative VAS scores to tactile and evaporative stimuli [Tables 3 and 4]. Uno group was significantly better to evaporative stimuli immediately ($P$ = 0.01) after application. After 1 week, Uno group was significantly better to tactile ($P$ = 0.000) and evaporative ($P$ = 0.000) stimuli.

DISCUSSION

The present study was the first to compare a fluoride-containing desensitizing agent with a bio-polymer containing desensitizer. SEM analysis of dentin surfaces after the application of Profluorid and Uno demonstrated dentin tubular occlusion. Although there was a high degree of dentin tubular occlusion 1 h after application, there was a reduction in the number of occluded tubules and an increase in the number of open tubules after 24 h for both materials. When clinical reduction of hypersensitivity was compared between Uno and Profluorid, it was found that at the evaporative evaluation performed immediately after application, Uno was significantly better. The first null hypothesis was rejected since both the agents tested significantly reduced sensitivity with a single application both immediately and at the 1-week recall. At the 1 week tactile and evaporative evaluation, sensitivity reduction due to the application of Uno was significantly better. The second hypothesis was only accepted for results obtained with tactile evaluation immediately after application.

Table 3: Comparison between different treatment groups using tactile stimuli

| Time interval | Group       | n  | Mean rank | Sum of ranks | P     |
|---------------|-------------|----|-----------|--------------|-------|
| Preoperative  | UNO         | 30 | 29.00     | 870.00       | 0.394 |
|               | Profluorid   | 30 | 32.00     | 960.00       |       |
| Immediate     | UNO         | 30 | 30.50     | 915.00       | 1.000 |
|               | Profluorid   | 30 | 30.50     | 915.00       |       |
| 1 week        | UNO         | 30 | 16.00     | 480.00       | 0.000*|
|               | Profluorid   | 30 | 45.00     | 1350.00      |       |

*Highly significant. Mann-Whitney U-test

Hence, the second hypothesis was not accepted for evaporative results obtained immediately after application and for results obtained for both tactile and evaporative stimuli at the 1 week recall.

In this study, the VAS was used to evaluate baseline sensitivity as well as sensitivity immediately after the application of desensitizers and at the 1-week recall. VAS can be used to translate patient’s subjective feedback after tactile and evaporative stimuli into objective data.
Fluoride in the form of Sodium fluoride, Stannous fluoride, and Sodium monofluorophosphate has been used to treat dentin hypersensitivity.[8,23] Torres et al. have reported that a fluoride varnish containing 6% sodium fluoride and 6% calcium fluoride varnish is effective in the treatment of dentin hypersensitivity.[17] Immediate reduction of hypersensitivity in Profluorid Group may be due to the synthetic resin and solvents in Profluorid Varnish that can create a protective layer on exposed dentin. A further effect of Profluorid may be due to the dissolution of sodium fluoride and deposition of calcium fluoride that can occlude the dentinal tubules.[26] In this clinical trial, Profluorid Varnish containing 5% sodium fluoride, significantly reduced pain of dentin hypersensitivity immediately after application. Effective reduction of hypersensitivity was also seen at the 1-week recall, which correlated with a study done by Ravishankar et al.[22]

Patients also reported a significant reduction of hypersensitivity immediately after the application of Uno Gel with similar results at the 1-week recall. According to the manufacturers, Uno contains bio-active polymers (BioSchell™), which can occlude dentinal tubules.[14] Uno contains chitosan, which is a derivative of chitin, which contains poly (1,4-D-glucopyranosamine).[27] Currently, there is a degree of opposition to fluoridation due to the risk of possible toxicity.[28] Uno does not contain fluoride and can provide an alternative to fluoride mediated desensitization. Limitations of the present study include the short trial period of 7 days. Further studies with longer time periods may be recommended. In addition, using an in-situ model that may help in the further evaluation may be recommended.

CONCLUSIONS

Uno Topical Gel and Profluorid were effective in reducing hypersensitivity immediately after application and at the 1-week recall. However, Uno Topical Gel showed a better desensitizing effect in comparison to Profluorid on evaporative stimuli immediately after application and to both tactile and evaporative stimuli at the 1-week recall.

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Conflicts of interest

There are no conflicts of interest.

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