CLINICAL STUDY REPORT

INTRODUCTION

Restorative dental materials are used to prevent or repair damage to teeth caused by oral disease or trauma. Though the currently available restorative materials like glass ionomer cements, resin restorations etc. may serve the purpose by restoring the form and function of the tooth but lacks the bioactivity. Secondary caries caused by polymerization shrinkage and micro leakage are other major contributing factors for the failure of restorations. A micro gap formed due to the shrinkage may widen over a period due to changes in mechanical properties of materials and tooth making it inaccessible for maintaining oral hygiene thus making it favourable milieu for bacterial growth leading to secondary caries.

The longevity of dental restorations can be achieved by creating a tight bond to the tooth and a suitable environment for bacteria. Bonding agents with bioactive properties may provide a sealed interface by hydroxyapatite precipitation. Bioactive Glass has shown to induce dentin remineralisation. DentoClude F with Bioactive Glass as an active component and based on clinical studies data showed robust safety and efficacy, which suggest first in class device technology.

Dentinal hypersensitivity and inflammation due to exposed dentinal tubules is characterized by short, sharp pain in response to stimuli like thermal, tactile, osmotic, or chemical which cannot be ascribed to any other defect or disease. Various agents are available for the treatment of dental hypersensitivity either by partial or complete occluding of dentinal tubules, protein precipitation, anti-inflammatory action or sealing of the dentinal tubules.

DentoClude™ F contains Bioactive Glass with particle size of less than 1µm as the key ingredient designed to fill and block the dentin tubules. It reduces sensitivity by blocking open tubules with the unique formulation properties of silicon, sodium, magnesium, fluoride, calcium (Ca^{2+}) and phosphate (PO_4^{3-}) ions to promote optimum formation of Hydroxycarbonate apatite (HCA) which aids in preventing micro-leakage and dentinal hypersensitivity.

DentoClude™ F Tubule Agent must be used during the restoration of teeth. DentoClude™ F is applied to the exposed dentin and the solvent evaporated off, leaving the bioactive glass. DentoClude™ F is manufactured in such a way that it is intended to enter the exposed dentin tubules and penetrate to a greater depth that prevents micro-leakage and sensitivity.

INDICATION FOR USE

DentoClude™ F, a desensitizing agent for dentin surfaces by occluding dentin tubules to help prevent microleakage. Use DentoClude™ F under direct or indirect restorations following dentin etch and prior to dentin adhesive application. Use a DentoClude™ F as a desensitizing agent for use in treatment of cervical erosion in Class V restorations.

CLINICAL STUDES

Multiple clinical studies were conducted that demonstrated the safety, efficacy, and viscosity of DentoClude F gel. A Comparative Evaluation of Stannous Fluoride Gel, Gluma and DentoClude F Gel in the Treatment of Dentinal Hypersensitivity & Micro-Leakage was studied. Both In-vitro and In-vivo evaluations were performed in this double blinded study of 30 patients with dentinal hypersensitivity due to micro-leakage/ reflex sympathetic dystrophy symptoms. Patients were randomly assigned into 3 treatment groups: DentoClude F (Cumberland Biotherapeutics), Gluma Gel (Heraeus Kulzer) and Senolin Stannous Fluoride Gel (Indoco Remedies). Response to the treatment was evaluated by Visual analog scale (VAS), and Wong Backers Facial Rating scale (FRS) ranging from 1 to 10 before application, immediately after application, 1 week post application and 4 weeks follow-up visit using both VAS and FRS scales. The results of the study data based on VAS and FRS scales suggest that DentoClude F gel decreases sensitivity, inflammation, and sharp pain by blocking and sealing dentinal tubules in comparison to GLUMA and Sensolin.

A second clinical study was conducted to compare safety and efficacy of four marketed products containing Bioactive glass in the treatment of dentin hypersensitivity (DH). DentoClude F: containing bioactive glass including botanical excipients that has anti-infectives/ inflammation value which is indicated for Sensitivity/ micro-leakage/ Class V Restorations; Sensodyne: containing Potassium nitrate, strontium acetate/chloride with indications such as sensitivity, tooth whitening; Bioenamel: containing glycerite, Potassium Nitrate, Bioglass, Carbopol with Indications such as remineralization of de-mineralized tooth structure, post whitening sensitivity and sensitivity caused due to non-carious lesions and sensitivity after oral prophylaxis; Elenz which has fluoride containing bioactive glass with Indication as Anti-sensitivity. Ten individuals with moderate to severe dentin hypersensitivity and pain in at least one canine or premolar in the four quadrants with VAS score ≥ 5 were selected to participate in the study. Each quadrant in an individual was randomly assigned to one of the four agents containing Bioactive glass. Subjects received single application of the assigned agent. Results were assessed by visual analog scale and Schiff cold air sensitivity scale at baseline, immediately after the treatment, and after 4 weeks of the treatment. All the four agents showed some reduction in dentinal hypersensitivity after immediate application with significant reduction by DentoClude F gel. DentoClude F gel showed statistically significant reduction from baseline and in the 4-week treatment.

A third clinical study, conducted to evaluate the efficacy and safety of DentoClude F gel in the reduction of dentin hypersensitivity in a randomized, double-blind, split mouth clinical trial. This clinical study enrolled 20 subjects with dentinal hypersensitivity symptoms positive to air blast stimuli, cold stimuli and tactile stimuli and having a VAS score of 4 and above were recruited in the study. Caries-free patients who had at least 2 cervical lesions with clinical diagnosis of moderate to severe dentin hypersensitivity, adequate oral hygiene,

absence of periodontal disease or parafunctional habits were considered as eligible for this study. The quadrants in all the subjects were randomly assigned into 2 groups and treated with DentoClude F gel and placebo gel respectively. The randomization was performed by placing all the selected teeth in a list and assigning its treatment according to a predefined sequence. The DentoClude F gel and placebo were applied by one experienced Dental Study, other than the Principal Investigator, as follows: water rinse; dentin prophylaxis to remove gross plaque accumulation; cotton isolation rolls; dentin drying with an air syringe; application of gel according to the manufacturer's instructions. The patients were instructed to avoid using any other desensitizing agent during the investigation. The response is evaluated by visual analog scale (VAS) ranging from 1 to 10 before the application, 1 week, 15 days, 30 days, and 45 days post application. Results were assessed at baseline, the VAS scores of test site and control site showed non-significant result with p value 0.61 which is ideal for a split mouth study. Intragroup analysis of VAS score in the test site between baseline to 45 days showed significant reduction in the VAS scores inferring reduction in hypersensitivity with a p- value of 0.0003.

This delivery application study compared the efficacy of DentoClude™ F gel with two different viscosities application to determine the appropriate and ideal viscosity gel as delivery application flow of the DentoClude™ F gel to the tooth surface while adequately viscous to remain at the targeted site of action for an adequate time at an effective concentration to perform its intended action. Twenty-four patients with mild, moderate to severe dentinal hypersensitivity symptoms were recruited in this study. Patients with the history of tooth hypersensitivity to thermal, mechanical, sweet, or sour stimuli on at least two teeth with a VAS score of at least 3; hypersensitive area on facial surfaces of the teeth; good physical health; and a willingness to participate in the study were recruited while chipped teeth, defective restorations, cracked tooth syndrome, fractured displaced cusps, deep periodontal pockets, or a tender tooth in the same quadrant as the hypersensitive teeth; orthodontic appliances, dentures, or bridgework that would interfere with the evaluation of hypersensitivity; taking antibiotics and/or anti-inflammatory drugs; already undergoing treatment for tooth hypersensitivity; deep dental caries or large restorations showing pulpal response; pregnant or lactating females; periodontal surgery within the previous 6 months; chronic systemic disease; or a pacemaker were excluded from the study.

These subjects were randomly assigned into 2 groups with 12 subjects each and treated with two different samples Sample 2 and Sample 3 of DentoClude™ F gel. The response was evaluated by visual analog scale (VAS) ranging from 1 to 10 before the application, immediately after application, 1week and 15 days post application. The teeth were isolated with cotton rolls and dried with cotton pledgets. A drop of desensitizer was then applied using cotton applicator and left for 2-3 minutes. For all the stimuli tests, patient response was recorded immediately after application and 1week and 15 days post application. A minimum gap of 5 minutes was given between each stimuli. Each test was repeated three times, and the average final score was recorded. The patients were instructed not to use any

other desensitizing agent during the study. All the analysis was performed using SPSS version 18. A p-value of <0.05 was considered statistically significant. Inter-group Comparisons were done using ANOVA with post-hoc Tukey's test.

Intergroup comparisons of Means and Standard deviations of VAS scores at different time intervals show statistically significant differences between VAS scores across all time point intervals except baseline. Intra group comparison of Means and Standard deviations of VAS scores within group 1(sample -3) at different time intervals shows significant differences between all pairwise comparisons except 1 week vs 15 days. Intragroup comparison of Means and Standard deviations of VAS scores within group 2 (sample 2) at different time intervals shows significant differences between all pairwise comparisons except 1week vs 15 days and immediate vs 15 days. Overall Sample 3 showed better viscosity when applied clinically and gave better reduction in VAS scores compared to sample 2. None of the subjects reported any adverse events to the treatment till date suggesting its safety.

DISCUSSION

Microleakage and Nano leakage is the seepage of fluids, debris, and/or microorganisms into micrometer-sized and nanometer-sized gaps between a dental restoration and tooth respectively. Without being held to the theory, the ability of bioactive glasses to promote the formation of apatite in aqueous environments that contain calcium and phosphate in saliva can facilitate inhibition of leakage at the bonded interface through a mechanism of self-sealing due to the formation of apatite.

DentoClude™ F contains Bioactive Glass with particle size of less than 1µm as the key ingredient designed to fill and block the dentin tubules preventing micro-leakage and dentinal hypersensitivity DentoClude™ F interacts with the oral biological environment to elicit a specific biological response, such as the formation of a hydroxyapatite layer with a bond forming between the tissue and material. It has superior surface area with a higher dissolution rate and thus faster hydroxyapatite formation and has been shown to increase the mechanical properties of such composite for natural bones and provide biomimetic nano-structuration enhancing cell adhesion. The current study proved that DentoClude™ F gel, Bioactive glass containing product is efficacious in reducing micro-leakage and dentinal hypersensitivity without unduly affecting the safety of the subject.

CONCLUSION

Dentine hypersensitivity is a frequently encountered patient complaint that can present with a number of associated factors including erosion and abrasion. The hydrodynamic mechanism responsible for dentine hypersensitivity is intimately related to the anatomical and physiological composition of teeth. Alterations to the integrity of the enamel and dentine through processes of trauma, decay and tooth wear can increase dentine permeability. This

gives rise to symptoms of sensitivity as dentinal fluid movement in response to thermal, chemical, and mechanical cues stimulate the pulpal fibres.

DentoClude™ F gel application showed to be safe, tolerable and demonstrate efficacy in 4 weeks treatment application on the surface of the tooth with superior improvement in dentine sensitivity and cervical erosion/ restoration.