Comparison of the Efficacy of Two Different Desensitizing Agents: A Randomized Controlled Trial

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Abstract

Aim: To evaluate and compare the efficacy of oxalate-containing desensitizer BisBlock™ and glutaraldehyde-containing desensitizer Gluma®.

Materials and methods: A subject-blind randomized controlled trial was conducted among 50 adult patients of age ranging from 18 - 65 years who self-reported dentine hypersensitivity. Each participant with at least one tooth with hypersensitivity in two different quadrants and showing a response of ≥ 3 on a visual analogue scale (VAS) to an evaporative stimulus was included in the study. The teeth were evaluated immediately after treatment, and after 24 hrs, one week, one month and 3 months from the baseline after application of BisBlock™, an oxalate-containing desensitizer, and Gluma®, a glutaraldehyde-containing desensitizer.

Results: Fifty participants were enrolled in the study. Means and standard deviations of VAS scores were calculated. The level of significance was set to $p < 0.05$. Statistically significant reduction in mean scores was found after application of Gluma® and BisBlock™ desensitizer ($p < 0.001$) at all time intervals. BisBlock™ yielded a statistically significant greater reduction in dentine hypersensitivity at 1 week ($p < 0.05$) and 1 month ($p < 0.01$) with evaporative stimulus.

Conclusion: Compared with Gluma®, BisBlock™ gave statistically significantly greater reduction in hypersensitivity.

Keywords: Dentine hypersensitivity, non-carious cervical lesions, Gluma® varnish, BisBlock™ , VAS, evaporative stimulus, thermal stimulus

Introduction

Dentine hypersensitivity (DH) is a relatively common dental clinical condition in permanent teeth caused by dentine exposure to the oral environment as a consequence of loss of enamel and/or cementum. It is characterized by short, sharp pain arising from exposed dentine, in response to tactile, evaporative, chemical or thermal stimuli that cannot be ascribed to any other dental defect or pathology (Addy *et al.*, 1992; Walters, 2005). The prevalence of DH has been reported to range from 4 to 74% among the population in the age range of 20-30 years, depending on the population studied, study settings, and study design (Bartold, 2006; Miglani *et al.*, 2010). The overall prevalence was found to be 26% in a study conducted in Southern India, and it was highest among the 35-50 years age group (Hegde and Bhalla, 2009). The need for desensitizing treatment may vary with sex, *i.e.* females tend to be more often affected with DH than males (de Assis *et al.*, 2006; Duran and Sengun, 2004).

The goal of treating dentine hypersensitivity is the immediate and permanent cessation of pain. Extensive research has been done on the management of hypersensitive dentine, but no treatment is accepted universally. Sealing the dentinal tubules with a bonding agent or adhesive material has been suggested to create long-lasting blockage of dentine hypersensitivity (Brännström *et al.*, 1979).

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One such product is "Gluma® Desensitizer" (Heraeus Kulzer GmbH, Hanau, Germany), composed of 5% glutaraldehyde and 35% hydroxyethyl methacrylate (HEMA). Glutaraldehyde acts as a very effective biological fixative and forms a physiological seal by coagulating the plasma proteins in the dentinal tubules. Similarly, HEMA also has an ability to infiltrate into acid-etched moist dental hard tissues and induce precipitation of serum proteins within tubules, thus achieving tubule occlusion and alleviating dentine hypersensitivity (Burke and Malik, 2000; Schupbach *et al.,* 1997).

On the other hand, BisBlock™ desensitizer" (Bisco, Inc., Schaumburg, IL, USA) is an oxalic acid-containing desensitizing agent. It reacts with the calcium of dentine to form insoluble, acid-resistant calcium oxalate crystals that cause tubule occlusion, reduce dentinal permeability and make the dentin more resistant to dissolution after treatment (Cunha-Cruz *et al.,* 2011; Pereira *et al*., 2005).

Many clinical studies (Brahmbhatt *et al*., 2012; Camilotti *et al*., 2012; de Assis *et al*., 2006; Dondi Dall'Orologio *et al*.,1999; Dondi Dall'Orologio *et al*., 2002; Duran, 2004; Jalalian *et al*., 2009; Olusile *et al*., 2008; Ozen *et al*., 2009; Pamir *et al*., 2007; Sethna *et al*., 2011; Vora *et al*., 2012; Mehamood *et al.,* 2011) have been conducted to determine the potential role of Gluma® and BisBlock™ as effective desensitizing agents. However, there are no studies reported in the literature comparing the efficacy of these two desensitizing agents for the treatment of dentine hypersensitivity. Thus, the present study was undertaken with the objective of comparing the efficacy of these two desensitizing agents.

Subjects and methods

A split-mouth randomized clinical trial was conducted among patients recruited from the V.S Dental College and Hospital, Bengaluru, Karnataka, India from October 2012 to July 2013, until the desired sample size was achieved. Subjects were between 18 to 65 years of age with a history of tooth hypersensitivity to thermal, mechanical, sweet or sour stimuli who had at least one tooth with hypersensitivity in two different quadrants of the mouth. The teeth included were those with buccal gingival recession and exposed dentine > 2 mm from the cementoenamel junction (CEJ) and non-carious cervical lesions that elicited a response of ≥ 3 on a visual analogue scale (0-10) to an evaporative stimuli.

Exclusion criteria for subjects were allergies to any product ingredients, current use or use of professional desensitizing treatment in the 3 months prior to the study, eating disorders such as gastroesophageal reflux and bulimia nervosa, orthodontic treatment within the previous three months, or medically compromised patients. Excluded teeth were those with caries or restorations, deep periodontal pockets, pulpal involvement, and those with any kind of prosthesis or serving as abutment teeth.

Fifty adult subjects (31 males and 19 females) between 18-65 years of age and presenting with the chief complaint of DH in the out-patient department of Oral Medicine and Radiology at V.S Dental College and Hospital, Bengaluru, were recruited. The Institutional Review Board and ethical committee approved the study protocol, and written informed consent from each subject was obtained after explaining the nature of the study.

Study design

Each subject's oral cavity was divided into four quadrants; different agents were applied in two different quadrants with at least one sensitive tooth. A single trained examiner was responsible for applying both stimulus and desensitizing agents and collecting subjects responses during recall visits. Calibration of the examiner was not necessary for the assessment of study outcome, as the patients provided subjective responses.

In order to avoid bias, the subjects were blinded to the actual material received by them. Because the delivery methods differed for Gluma® (positive control) and BisBlock™ (test material), examiner blinding was not viable during the application phase, but was exercised during the follow-up visits. Both agents were randomly allocated to different quadrants.

Pain assessment

Pain was assessed in response to the following stimuli: 1) Evaporative method – a short air blast was applied from a three-way air syringe from the dental unit for 5 seconds at a distance of 0.5 cm from the tooth surface; 2) Thermal method - a disposable syringe with a 0.5 mm diameter needle was used to apply 0.5 ml freshly melted ice cold water (up to 10º C) for 10 seconds with the tip at a 2 mm distance from the tooth.

The order of application of stimulus was such that the least disturbing stimulus was applied first (thermal stimulus), with the most disturbing (evaporative stimulus) applied last. The order in which the teeth were treated was randomized. Both stimuli were applied on the cervical region of the experimental teeth and neighbouring teeth were isolated during testing using the operator's fingers and cotton rolls.

The subjects were asked to rate their overall sensitivity to a blast of air and to cold water application by marking a point on the VAS scale. If the discomfort became intolerable the stimulus was immediately removed. Throughout the study, the test stimuli were applied in the same order, with minimum 5-minute interval between the applications of different stimuli.

The pain was assessed in test and control teeth at the baseline visit before application of the agent and immediately after application, 24 hrs, one week, one month and 3 months from the baseline.

Procedure

After baseline pain assessment, the two selected hypersensitive teeth were randomly assigned by means of lottery method to test or control. The test tooth was treated with BisBlock™ desensitizer and the tooth treated with Gluma® desensitizer served as a positive control. The application of material was in accordance with the manufacturer's instructions.

Patients were advised to use their standard dentifrice without any desensitizing component and their conventional toothbrush. In case of inefficacy of the agents used in the study, bonded resin composite or glass ionomer restoration was performed. A visual soft-tissue examination was also performed at every recall visit and any soft tissue irritation was recorded by the examiner.

Statistical analysis

Analysis of the data was done using SPSS version 18. Means and standard deviations were calculated and the Mann-Whitney U test was used to compare mean VAS scores between the two agents for each of the assessments of pain from evaporative and thermal stimuli. Comparison of mean VAS scores between different time intervals with both agents for both stimuli was assessed using Wilcoxon signed rank test. The level of significance was $p < 0.05$.

Results

Fifty participants were enrolled in the study, of which 62% were males and 38% females. The mean age of study participants was 43.62 years (standard deviation 10.06). Dentine hypersensitivity peaked between 33- 54 years, followed by a decline with age. Comparison of the performance of two desensitizing agents in the VAS response to evaporative and thermal stimuli indicated that both agents (BisBlock™ and Gluma®) were effective in alleviating dentine hypersensitivity at all time intervals compared to baseline. BisBlock™ yielded a statistically significant greater reduction in DH at 1 week ($p < 0.05$) and 1 month ($p < 0.01$) with evaporative stimulus (Mann-Whitney U test; *Table 1, 2*).

Although there was a reduction in the mean VAS scores in both males and females from baseline to other time intervals with both stimuli, the difference in the values did not reach a statistically significant level (Wilcoxon signed rank test).

Discussion

Dentinal hypersensitivity is a problem that plagues many dental patients. Selection of the correct treatment modality is based on the premise of proven clinical efficacy both in terms of magnitude and duration of desensitizing effect. Lack of proven universal acceptance of any one such treatment creates the need for a comparative analysis of the most commonly accepted desensitizing treatments.

In the present study, males were higher in number (62%) compared to females (38%), which is in contrast to the studies done by de Assis (2006) and Duran (2004). The perception to desensitizing treatment may vary with sex; *i.e.*, females tend to be more often affected with DH than males. The higher prevalence of DH in this gender might be related to heightened oral hygiene awareness in women, which leads to excessive oral hygiene habits such as aggressive tooth brushing (de Assis, 2006; Duran, 2004). However, no variation in the perception of DH was reported in the present study. There was a reduction in the mean VAS scores in both males and females with both agents, but the differences were not statistically significant.

Table 1. Mean visual analogue scale (VAS) scores with evaporative stimulus

Evaluation	Gluma®	BisBlock™	*p* values
Before application	4.48 ± 1.75	4.90 ± 1.83	0.122
After application	1.36 ± 1.27	1.56 ± 1.47	0.638
24 hrs post-treatment	1.24 ± 1.05	1.27 ± 1.17	0.891
One week post-treatment	1.51 ± 1.08	0.98 ± 1.01	0.010*
One month post-treatment	1.31 ± 0.85	0.86 ± 0.91	0.008*
Three months post-treatment	1.22 ± 0.77	0.98 ± 0.81	0.156

*Denotes significant difference (Mann-Whitney U test)

Table 2. Mean visual analogue scale (VAS) scores with thermal stimulus

Evaluation	Gluma®	BisBlock™	*p* values
Before application	4.52 ± 1.54	5.04 ± 1.85	0.147
After application	0.68 ± 1.30	0.98 ± 1.57	0.338
24 hrs post-treatment	1.02 ± 1.33	0.96 ± 1.08	0.776
One week post-treatment	0.98 ± 1.16	1.12 ± 1.09	0.359
One month post-treatment	1.04 ± 1.06	0.67 ± 0.83	0.061
Three months post-treatment	0.78 ± 0.85	0.69 ± 0.79	0.645

No statistically significant differences (Mann-Whitney U test)

Although it is believed that cervical dentine exposure increases with age, the present study showed that DH peaked between 33- 54 years, followed by a decline with age. These findings are in agreement with previous studies (Brahmbhatt *et al*., 2012; Camilotti *et al.,* 2012; Chabanski *et al*., 1997; Cuenin *et al*., 1991; Bahsi *et al*., 2012; Gillam *et al*., 2004; Fischer *et al.,* 1992; Flynn *et al*., 1985; Rees *et al*., 2004; Vora *et al*., 2012).

The probable reason for this drop in DH after the 5th decade may be related to changes that occur in the dentine pulp complex with increasing age, particularly dentinal sclerosis and the laying down of secondary or tertiary dentine that causes a reduction in dentine permeability (Chabanski *et al*., 1997).

Presently, there is no agent or product for sensitive teeth that can be considered as a gold standard. However, Ide *et al.* (1998) suggested that a dentine-bonding agent containing HEMA and polycarboxylic acid may be considered as a gold standard and thus can be used for both assessment of techniques for estimating cervical sensitivity and for estimating the efficacy of professionally applied topical desensitizing agents. Gluma® desensitizer was therefore used as a positive control in the present study.

Duran and Sengun (2004) compared the effectiveness of five desensitizer products, including the Gluma® desensitizer and found VAS scores significantly decreased compared to baseline. Dondi dall'Orologio *et al.* (2002) found Gluma® desensitizer to be successful in a non-controlled trial. On comparative analysis by Brahmbhatt (2012), Gluma® showed better immediate effect as compared to topical 2% sodium fluoride at baseline, 2 weeks, 1 month and 3 months. This is likely to be due to the intra-dentinal sealing observed with Gluma®, unlike sodium fluoride, which takes time to form calcium fluoride crystals. Aranha *et al.* (2009) found that Gluma® desensitizer showed an immediate effect after application and the level of sensitivity remained the same until the 6-month follow-up. Schupbach *et al.* (1997) reported that the significant effect of Gluma® is attributed to glutaraldehyde, which is an effective fixative or flocculating agent with the capacity to form a coagulation plug within dentinal tubules; this may counteract the hydrodynamic mechanism of dentine hypersensitivity and bring about tubule occlusion up to a depth of 50 to 200 μm. Kanaparthy and Kanaparthy (2011) concluded that Gluma® desensitizer and G.C. tooth mousse have a more long-lasting effect when compared to amorphous calcium phosphate. However, whereas Gluma® desensitizer achieved its desensitizing action in a single application, multiple applications were required for G.C. tooth mousse in reducing sensitivity.

Olusile *et al.* (2008) showed reduction in the mean VAS for teeth treated with Gluma® after 7 days from the baseline. Similar results were reported by Mehamood *et al.* (2011) and Duran and Sengun (2004), and it was seen that Gluma® desensitizer was a better agent in relieving dentinal hypersensitivity than Duraphat in non-carious cervical lesions. On the contrary, Vora *et al.* (2012) reported the consistently greatest pain reduction with Gluma® power gel, which was followed by placebo, and the least pain reduction with BisBlock™.

In the present study, superior results were obtained with BisBlock™ desensitizer at 1 week and 1 month post-treatment, which may be attributed to deposition of calcium oxalate crystals on the dentine surface and/or inside its tubules, significantly reducing hydraulic conductivity inherent to this structure, sealing the tubules more effectively than the intact smear layer.

Similar results were reported by Camilotti *et al.* (2012), in which potassium oxalate gel presented a statistically significant reduction in sensitivity between the first and third weeks of evaluation. Significant reduction in dentine hypersensitivity after 21 days of potassium oxalate application was also found in studies by Pillon *et al.* (2004) and Assis *et al.* (2011).

Camps *et al.* (2003) reported an oxalate-desensitizing agent to be more effective than the placebo solution in decreasing the sensitivity both to air blast and to scratching. Oxalates form precipitates within dentine tubules that block dentinal fluid flow (Cuenin, 1991) and they have an added advantage of relative insolubility in acid, making them resistant to dissolution after treatment (Pereira *et al*, 2005; Pillon *et al.,* 2004). On the contrary, no significant reduction in desensitizing effect of Oxa-Gel from baseline up to first month of application was seen in a study by Aranha *et al.* (2009).

Although the strengths of the present study being use of a randomized controlled trial, application of materials by single operator, use of larger sample size and employing a split mouth study design (minimizing the effects of inter-patient variability), the study has a few limitations. Because a single examiner was responsible for both application of materials and recording of response to stimulus, bias on the part of the examiner cannot be excluded. Also, the follow-up period was only 3 months.

Conclusion

Within the limits of the present study, it may be concluded that a single application of both a glutaraldehyde-containing desensitizer and an oxalate-containing desensitizer were effective in reducing dentine hypersensitivity. This reduction in DH appeared immediately after application and persisted throughout the study duration, *i.e.*, for at least 3 months. Also, reduction in symptoms of hypersensitivity was greater in teeth treated with BisBlock™ as compared to those to which Gluma® desensitizer was applied.

Although many therapies aim to treat DH, there is no agent that is able to effectively obliterate the dentine tubules because the substances used are lost over time and require multiple applications. Topical desensitizing varnishes may be an important modality in treatment of DH, and a more prospective approach coupled with scientific research should be undertaken to evaluate their potential role as desensitizing agents.

References

Addy M and Urquhart E. Dentine hypersensitivity: its prevalence, aetiology and clinical management. *Dental Update* 1992; **19**:407-412.

Aranha AC, Pimenta LA and Marchi GM. Clinical evaluation of desensitizing treatments for cervical dentin hypersensitivity. *Brazil Oral Research* 2009; **23**:333-339.

Assis JS, Rodrigues LK, Fonteles CS, Colares RC, Souza AM and Santiago SL. Dentin hypersensitivity after treatment with desensitizing agents: a randomized, double-blind, split-mouth clinical trial. *Brazil Dental Journal* 2011; **22**:157-161.

Bahşi E, Dalli M, Uzgur R, Turkal M, Hamidi MM and Colak H. An analysis of the aetiology, prevalence and clinical features of dentine hypersensitivity in a general dental population. *European Review for Medical Pharmacological Sciences* 2012; **16**:763-769.

Bartold PM. Dentinal hypersensitivity: a review. *Australian Dental Journal* 2006; **51**:212-218.

Brahmbhatt N, Bhavsar N, Sahayata V, Acharya A and Kshatriya P. A double blind controlled trial comparing three treatment modalities for dentin hypersensitivity. *Medicina Oral, Patologia Oral y Cirugia Bucal* 2012; **17**:e483-490.

Brannstrom M, Johnson G and Nordenvall KJ. Transmission and control of dentinal pain: resin impregnation for the desensitization of dentin. *Journal of the American Dental Association* 1979; **99**:612-618.

Burke FJT and Malik R. Treatment of dentinal hypersensitivity using dentin bonding system. *International Dental Journal 2000*; **50**:283-288.

Camilotti V, Zilly J, Busato Pdo M, Nassar CA and Nassar PO. Desensitizing treatments for dentin hypersensitivity: a randomized, split-mouth clinical trial. *Brazilian Oral Research* 2012; **26**:263-268.

Camps J and Pashley D. *In vivo* sensitivity of human root dentin to air blast and scratching. *Journal of Periodontology* 2003; **74**:1589-1594.

Chabanski MB, Gilliam DG, Bulman JS and Newman HN. Clinical evaluation of cervical dentine sensitivity in a population of patients referred to a specialist periodontology department: a pilot study. *Journal of Oral Rehabilitation* 1997; **24**: 666-672.

Cuenin MF, Scheidt MJ, O'Neal RB, Strong SL, Pashley DH and Horner JA. An *in vivo* study of dentin sensitivity: the relation of dentin sensitivity and the patency of dentin tubules. *Journal of Periodontology* 1991; **62**:668-673.

Cunha-Cruz J, Stout JR, Heaton LJ and Wataha JC. Dentin hyper sensitivity and oxalates: a systematic review. *Journal of Dental Research* 2011; **90**:304-310.

de Assis Cde A, Antoniazzi RP, Zanatta FB and Rösing CK. Efficacy of Gluma® Desensitizer on dentin hypersensitivity in periodontally treated patients. *Brazilian Oral Research* 2006; **20**:252-256.

Dondi dall'Orologio G, Lorenzi R, Anselmi M and Opisso V. Dentin desensitizing effects of Gluma® Alternate, Health-Dent Desensitizer and Scotchbond Multi-Purpose. *American Journal of Dentistry* 1999; **12**:103-106.

Dondi dall'Orologio G, Lone A and Finger WJ. Clinical evaluation of the role of glutaraldehyde in a one-bottle adhesive. *American Journal of Dentistry* 2002; **15**:330-334.

Duran I and Sengun A. The long-term effectiveness of five current desensitizing products on cervical dentine sensitivity. *Journal of Oral Rehabilitation* 2004; **31**:351-356.

Fischer C, Fischer RG and Wennberg A. Prevalence and distribution of cervical dentine hypersensitivity in a population in Rio de Janeiro. *Brazilian Journal of Dentistry* 1992; **20**:272-276.

Flynn J, Galloway R and Orchardson R. The incidence of 'hypersensitive' teeth in the West of Scotland. *Journal of Dentistry* 1985; **13**:230-236.

Gillam DG, Newman HN, Davies EH, Bulman JS, Troullos ES and Curro FA. Clinical evaluation of ferric oxalate in relieving dentine hypersensitivity. *Journal of Oral Rehabilitation* 2004; **31**:245-250.

Hegde M and Bhalla N. The prevalence of dentine hypersenstivity in Southern India. *Journal of the Indian Dental Association* 2009; **3**:1-6.

Ide M, Morel AD, Wilson RF and Ashley FP. The role of a dentine-bonding agent in reducing cervical dentine sensitivity. *Journal of Clinical Periodontology* 1998; **25**:286-290.

Jalalian E, Meraji N and Mirzaei M. A comparison of the efficacy of potassium nitrate and Gluma® desensitizer in the reduction of hypersensitivity in teeth with full-crown preparations. *Journal of Contemporary Dental Practice* 2009; **10**:66-73.

Kanaparthy R and Kanaparthy A. Clinical efficacy of amorphous calcium phosphate, G.C. tooth mousse and Gluma desensitizer in treating dentin hypersensitivity. *International Journal of Dental Clinics, North America* 2011; **3**. Available at: <http://intjdc.com/index.php/intjdc/article/view/66>.

Mehamood Z, Shah JA, Javed MU, Manzoor MA, Asghar I and Saeed MH. Efficacy of Gluma® desensitizer and Duraphat in relieving dentine hypersensitivity in non-carious cervical lesions. *Pakistan Oral and Dental Journal* 2011; **31**:183-186.

Miglani S, Aggarwal V and Ahuja B. Dentine hypersenstivity: Recent trends in management. *Journal of Conservative Dentistry* 2010; **13**:218-224.

Olusile AO, Bamise CT, Oginni AO and Dosumu OO. Short-term clinical evaluation of four desensitizing agents. *Journal of Contemporary Dental Practice* 2008; **9**:22-29.

Ozen T, Orhan K, Avsever H, Tunca YM, Ulker AE and Akyol M. Dentin hypersensitivity: a randomized clinical comparison of three different agents in a short-term treatment period. *Operative Dentistry* 2009; **34**:392-398.

Pamir T, Dalgar H and Onal B. Clinical evaluation of three desensitizing agents in relieving dentin hypersensitivity. *Operative Dentistry* 2007; **32**:544-548.

Pereira JC, Segala AD and Gillam DG. Effect of desensitizing agents on the hydraulic conductance of human dentin subjected to different surface pre-treatments - an *in vitro* study. *Dental Materials* 2005; **21**:129-138.

Pillon FL, Romani IG and Schmidt ER. Effect of a 3% potassium oxalate topical application on dentinal hypersensitivity after subgingival scaling and root planing. *Journal of Periodontology* 2004; **75**:1461-1464.

Rees JS and Addy M. A cross-sectional study of buccal cervical sensitivity in UK general dental practice and a summary review of prevalence studies. *International Journal of Dental Hygiene* 2004; **2**:64-69.

Schupbach P, Lutz F and Finger WJ. Closing of dentinal tubules by Gluma® desensitizer. *European Journal of Oral Sciences* 1997; **105**:414-421.

Sethna GD, Prabhuji ML and Karthikeyan BV. Comparison of two different forms of varnishes in the treatment of dentine hypersensitivity: a subject-blind randomised clinical study. *Oral Health and Preventive Dentistry* 2011; **9**:143-50.

Vora J, Mehta D, Meena N, Sushma G, Finger WJ and Kanehira M. Effects of two topical desensitizing agents and placebo on dentin hypersensitivity. *American Journal of Dentistry* 2012; **25**:293-298.

Walters PA. Dentinal hypersensitivity: a review. *Journal of Contemporary Dental Practice* 2005; **6**:107-117.