

Investigating the Effect of 45S5 Bioactive Glasses and Calcium Oxalate (Gluma) Covering the Dentinal Tubules in Dental Sensitivity

Elnaz Shafiq¹, Reza Fekrazad², Mahdi Shafikhani^{3*}

¹Assistant Professor, Recovery Specialist, Faculty Member, Faculty of Dentistry, Army University of Medical Sciences, Tehran, Iran.

²Full Professor, periodontologist, Faculty Member, Faculty of Dentistry, Army University of Medical Sciences, Tehran, Iran.

³Dentistry Student, Faculty of Dentistry, Army Medical University, Tehran, Iran.

*Corresponding Author

ABSTRACT

Introduction & Objective: Increased clinical dentin hypersensitivity is seen among 30-40-year-olds. This complication is directly related to the size of the dentinal tubules. Therefore, considering the importance of dental sensitivity control and finding newer and more mundane ways to control it. The purpose of this study was to investigate the effect of bioglass 45S5 and calcium oxalate (gluma) for covering the dentinal tubules in dental sensitivity.

Methods: This experimental and laboratory study was conducted at the Army Dentistry School in 2019, after obtaining permission from the Ethics Committee of the Army Medical University. For this study, 45 premolar and healthy molars were collected from the surgery department of the Army Dentistry School. The teeth lacked any restorations, caries, or cracks. Samples were randomly assigned into three equal groups using the random numbers table. A group was treated with bioglass, a group treated with gluma (calcium oxalate), and a group was as the control group. After collecting data from the samples using a questionnaire, the information was encrypted and entered into the computer. Then, using SPSS software, one-way analysis of variance was used to analyze the data. Normality analysis of the mean distribution was performed using the Kolmogorov-Smirnov test. In all tests, the significance level was considered to be 0.05.

Results: Both gluma and bioglass materials were effective and significantly filled dentin tubules more than control group thus can effectively reduce dental sensitivity. On the other hand, the results showed that Bioglass is significantly more effective than gluma. It causes dentinal tubules to fill up. So, in SEM images, Bioglass in few samples closed all dentin tubules; therefore, it seems to be more effective in reducing dental sensitivity.

Conclusion: According to our results, both bivalve cells and gluma had a significant effect in dentin tubules compared to the control group. In addition, Bioglass is a more effective anti-allergic agent than gluma.

Keywords

Bioaccumulation Glass, 45S5, Calcium Oxalate, Dentin Tubules, Dental Sensitivity

Introduction

Dental sensitivities are one of the most common dental problems that are often caused by the presence of ducts (tubules) in the dentins. In normal conditions, dentin is covered by enamel and cement and is not affected by stimuli. It occurs only when facing with peripheral nerve terminals in dentinal tubules, known as dentin hypersensitivity. This sensitivity is specified by short and spasmodic pain due to thermal or chemical stimulation (osmotic) or tactile stimulation (1), and it cannot be attributed to any other pathology (2). The increased dentinal hypersensitivity is more common among people aged 30-40 years and its maximum prevalence is in the third decade of life (3, 4). The prevalence of the problem is among 4-73% of normal individuals and 60-98% of periodontal patients (5-8). The difference in the prevalence may be due to different diagnostic methods (9). The prevalence of dental hypersensitivity (DH) is more common after periodontal treatments and it is between 72.5% and 98% (10). The prevalence is higher in women than in men, apparently due to better care and more treatment apply for women (3, 11, and 12). The increased sensitivity is mostly observed in the buccal area of the permanent teeth, and it is more prevalent in canines, first premolar, incisors, second premolars, and molars. The pain caused by dentinal sensitivity is sharp, localized, and short-term (6, 13). Sensitive dentin is associated with the oral environment due to one or both mechanisms of the enamel removal and exposure to the root surface or loss of cement covering and periodontal tissues (14, 15). The gingival reduction is the most common clinical cause of exposure to dentinal tubules (4). There are two theories in the case of dentinal hypersensitivity. The first theory expresses that the cause is neural structures in dentinal tubules and peripheral odontoblasts and processes in them (16). The second theory (hydrodynamic theory) states that the change in the fluid flow of dentinal tubules, as well as the indirect stimulation of pulpal neural terminals, is the reason for sensitivity while the decreased number or diameter of open dentinal tubules results in increased dentin hypersensitivity (6, 17). The stimulated nerves are indeed the δ A neuronal fibers located in the

dental tubules (18). The activity of these nerves depends on the openness or closure of dental tubules. DH is directly associated with the size of the dental tubules (2). The fundamental factor in DH generation is the absence of enamel or cement on the root surface and dentin exposure (19). Thus, the cervical area of the teeth is the most common hypersensitive area (2). In order to detect DH, a probe or airway pump can be used to stimulate the patient's response (22). There are often two general clinical guidelines to reduce dental hypersensitivity; first, reducing the ability of the pulpal nerves in responding to dentinal fluid changes, and the other reducing the stimuli of the motion of dentin fluid through reducing dentinal penetrability (16). To this end, various materials such as silver nitrate, stannous fluoride, sodium fluoride, calcium oxalate, and resins and strontium chloride are used to cover the open dental tubules (17). Plaque control is a very significant factor in controlling dentinal sensitivity. The presence or absence of plaque in the opening of the dental tubules is very effective. Kawasaki's study (2001) revealed that when the plaque control plan was removed, the diameter of dental tubules enhanced by three times their original size over three weeks, and when the plaque was controlled, the diameter of these tubules decreased to 20% of their initial diameter within one week (21). In recent years, these sensitivities have become more prevalent with an increased desire for long-term maintenance of teeth, and they may occur at any age and in both genders (23, 24).

No study has been so far presented that is able to provide an ideal treatment satisfying 100% of patients. This is because of problems in the method of standardization of the stimuli and their response, undermining a very precise study. Of course, various treatments have been recommended, such as dietary recommendations, proper brushing training, occlusion adjustment, use of adhesive systems, adhesive restorations, use of anti-allergic products and salts like potassium ions, oxalate, and sodium fluoride, the use of low and high power lasers for DH therapy (21). Available materials to treat dental hypersensitivity include those affecting nerves such as potassium nitrate and dentinal tubular blockers, including ions, salts containing stannous fluoride, sodium fluoride/stannous fluoride combination, potassium oxalate, ferrous oxide, strontium chloride, amino acids/proteins, such as glutaraldehyde, resins, like dentin sealers and methyl methacrylate (25). Gluma desensitizer is a combination of glutaraldehyde and (Hydroxyethyl)methacrylate. Glutaraldehyde causes the coagulation of proteins and amino acids within the tubules and, also, it is an effective disinfectant. Furthermore, HEMA can be effective in the closure of dental tubules. Gluma desensitizer has no interference in adhesion to dentinal structures; however, its drawback is that due to the presence of glutaraldehyde, it leads to injury to the gum after long-term contacting with it and, due to the presence of HEMA, it can cause contact dermatitis, and, it incidentally has the ability piercing of latex gloves (23, 25). Thus, we should note to its use and it is better to use Rubber Dam (26). Meanwhile, this substance is soluble in water, resulting in its deep penetration in the dental tubules. The effect of this substance is reversible, it gradually loses its effect, and dental tubules will reopen (23). In 2005, Pamir et al. compared the three materials of potassium nitrate 5%, sodium fluoride 2%, and Pop L prompt, and concluded that the temperature stimulants cause the patients' discomfort more than mechanical stimuli and all three anti-susceptibility substances significantly decreased patients' discomfort against both temperature stimuli and mechanical stimuli (27). In 2003, Ferechoso Cuesta et al. performed a research, compared 5% and 10% potassium nitrate gel, and concluded that the 10% concentration of the mentioned material shows more reduced sensitivity after 48 hours and the difference between the effects of two concentrations of the substance after 96 hours was greatly increased. Meanwhile, they concluded that the durability of the effect of potassium nitrate gel is obviously 10% until four days (28) (29). In 2002, William Lockart carried out a research in which he used an ultra-high-speed device with air coolant to cut the teeth (28-30). Meanwhile, after cutting the teeth, they were stained with stannous fluoride (this substance is an antisusceptibility material, itself) with cotton (1, 23), and concluded that none of the samples experienced pulpal necrosis based on radiography evidence and no clinical symptoms was observed (100% success) (29, 30). It should be noted that, given the available papers, stannous fluoride itself is an interfering agent in decreasing dental hypersensitivity and, consequently, his findings cannot be documented so much. Pereira et al. (2002) compared the gluma and the oxagel on a pulled third molar tooth that had been cut and divided into four quadrants. In this investigation, electron microscopy (SEM) was used and it was concluded that both materials produced defective tubular obstruction. After etching the surfaces on which these materials were used, they observed that the etched surface on which the oxagel was used was like the untreated surface, but the etched surface, on which the gluma was used still had a defective obstruction (30). In 2000, Niazi compared the three pain-free, super seal, and gluma materials in reducing the sensitivity of the cut teeth, and concluded that all these substances reduced the sensitivity of the teeth, and the pain-free substance with the base of oxalic acid had less effect on reducing sensitivity to the cold stimulus (31).

The most important point in treatment is the selection of biologically active substances in the body with the ability to form stable bone marrow. Bioactivity may be defined as the ability of the material to form a solid structure in biological environments (32). Bioactive glass has mechanical specifications and high biocompatibility. Although

some studies indicate that due to the high thermal expansion coefficient of the bioactive glass and the tendency of these materials to crystallize during the heating process, they cannot be used alone as coatings for metal implants (33, 34). Bioactive glasses are one of the widely used biomaterials produced in 1969 by Hench et al. (35, 36). They are silicates, including sodium oxide, calcium, and phosphate, which, due to their ability to bind to soft and firm tissues of the body, are considered as one of the most important biomaterials used in medicine and dentistry for applications such as bone defect repair and jaw and facial renewal (37-39). It is noteworthy that the results of experiments on biocompatibility and the amount of formation of hydroxyapatite layer in such glasses showed that with the S45 compound, the bioactive glass has more bioactivity than the two 49S and 58S compounds (40).

Given the new application of bioactive glass in dentistry, as well as the necessity of identifying the clinical and laboratory effects of this substance in the treatment of dental sensitivities and the requirement of comparing its effects with highly functional substances like routine gluma, and considering the importance of dental hypersensitivity control and finding newer and more effective methods for controlling it, the present study aimed at investigating the effect of bioactive glass 45S5 and calcium oxalate on coating the dentinal tubules in dental hypersensitivity.

Method and Material

In this experimental and laboratory study conducted in Army Dentistry School in 2019, given the similar paper (41, 42), 45 healthy premolar and molar teeth pulled in the surgery department of the Army Dentistry School were collected. Considering the significance level of 5% and the test power of 80% and 0, and in order to achieve a minimum difference of 1%, and given the standard deviation of 65 points in the average rank of blocked dentinal tubules, 15 samples are needed in each group. Thus, the total number of samples was 45.

The teeth lacked any restorations, caries, or cracks. They were cleaned after being pulled and disinfected in the chloramine solution for 24 hours. The enamel of the teeth in the occlusal area was about 1 mm from the central fossa (measured by a graded probe) with a brown rough diamond disk (France, Bisico Co.) in order to make the dentine surface smooth for exposing; then, each of the samples was etched with 37% phosphoric gel (China, Dentex Co.) first, 15 seconds for dentin and 30 seconds for enamel (by total etching method) to open dentinal tubules (creating dental hypersensitivity conditions). Then, they were washed with distilled water for 30 seconds and were randomly divided into three equal groups using a random number table. A group was treated with bioglass, one group was treated with Gluma (calcium oxalate) and one group was the control group. The control group was maintained in distilled water unmodified until the end of the treatment. In the first group (bioglass group), the samples were brushed for 30 seconds a day and for 30 days with bioglass solution (containing nanoparticles made by Apatak Co., Yazd, Iran). After being brushed (using a medium-size micro-brush pen made by Panavia Co.) for 30 seconds, the air was mildly flushed from the distance of 20 cm to the occlusal surface of the tooth by the airway purar. For the second group (calcium oxalate group), just like the first group, the samples were stained with calcium oxalate (gluma produced by Kulzer Co., Germany). After the end of treatment, all three groups were sent to the laboratory (Lab FE_SEM Oil Institute of the University of Tehran) to evaluate the status of the dentinal tubules. The samples were mounted on a certain aluminum component, and the gold coating was conducted by a special vacuum device. Then, the micrographs were extracted from the components by an electron microscope with a magnification of 4500. The obtained micrographs were separately evaluated by two researchers. The Hulsmann index was ranked as follows (32, 33, 42).

Score 1- All dentinal tubules are open.

Score 2- More than 50% of dentinal tubules are open.

Score 3- Less than 50% of dentinal tubules are open.

Score 4- Almost all tubules are covered.

Any group that has covered more dentinal tubules than the control group has more ability to eliminate the sensitivity of the teeth. The data were collected from the studied sample by observation, and encoded and entered into the computer. They were then analyzed by SPSS software using one-way ANOVA. The assessment of the normality of means distribution was performed using the Kolmogorov-Smirnov test. In all tests, the significance level was considered 0.05.

Findings

According to the findings of the present study, the mean scores of the closure of tubules in the studied groups were statistically significant (Table 1). In addition, the mean scores of the closure of tubules in both groups of bioglass and gluma were higher than the control group and this difference was statistically significant. The mean of the closure of tubules in the bioglass group (fig 1) was higher than that of the gluma group (fig 2), and this difference was statistically significant, too (Table 2 and fig 3).

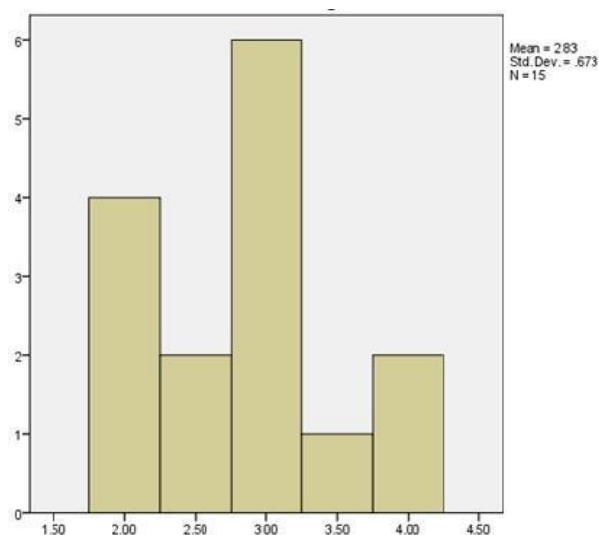


Fig 1) Distribution of tubules closure score in the bioglass group

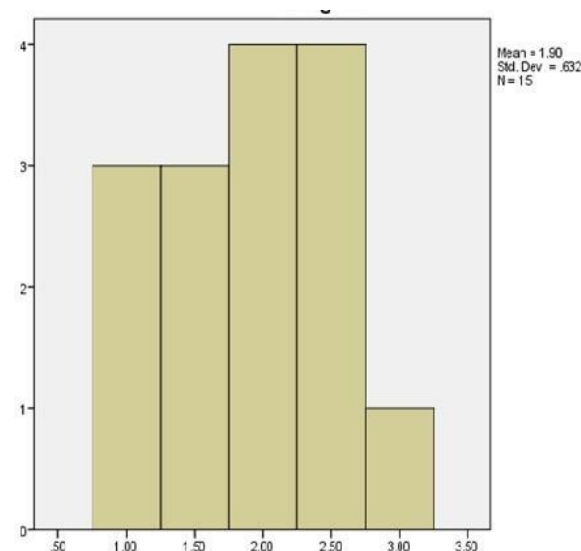


Fig 2) Distribution of tubules closure score in the gluma group

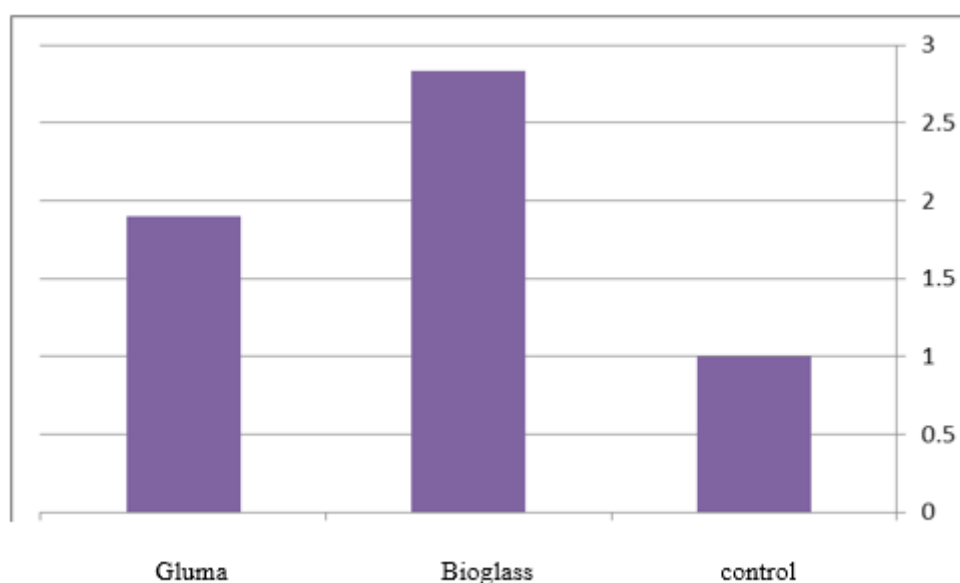


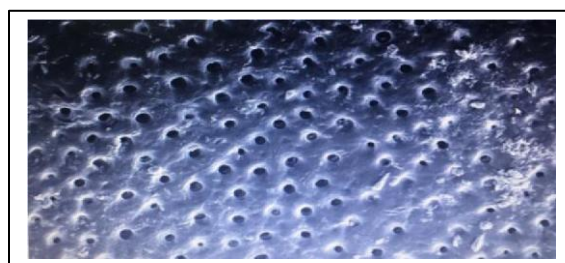
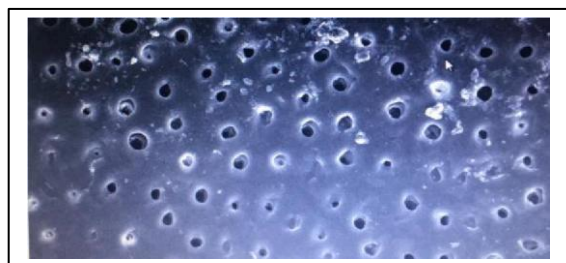
Figure 3: Comparison of the distribution of the score of the closure of tubules in the studied groups

Table 1: Comparison of the average score of tubules closure in one-way test (ANOVA).

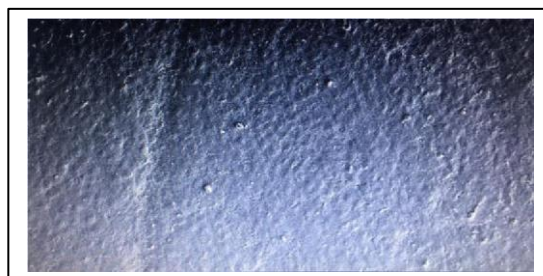
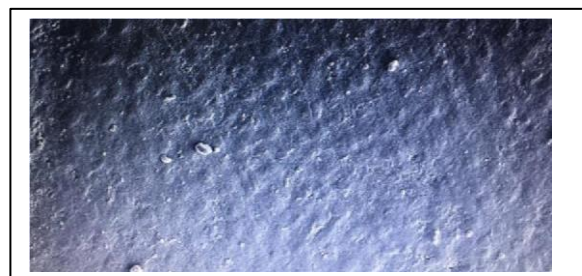
P-value	F	Squares of average	
0/001	44/36	12/6	Comparison between groups
		0/284	Intragroup comparison

Table 2 : The difference between the average closure of tubules in the LSD post hoc test

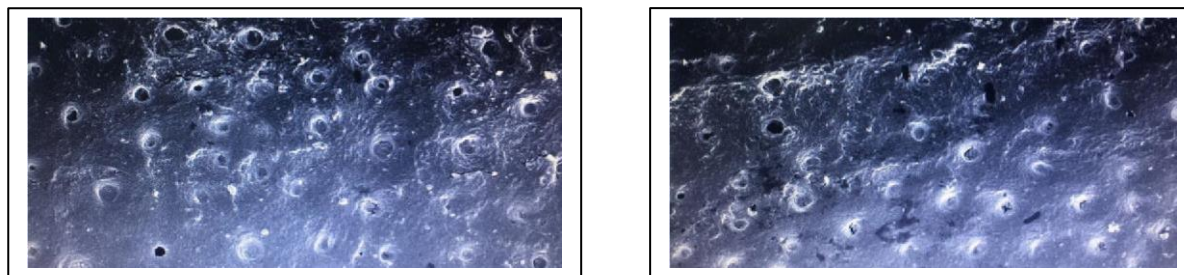
GroupI	Group J	Differences in average	Standard error	P value	95% confidence interval	95% confidence interval
					Down bond	Upper bond
Control	Bioglass	-1/83	0/19	0/005	-2/2	-1/5
	Gluma	-0/9	0/19	0/005	-3/3	-0/5
Bioglass	control	1/83	0/19	0/005	1/5	2/2
	gluma	0/93	0/19	0/005	0/5	1/3
gluma	control	0/9	0/19	0/005	0/5	1/3
	Bioglass	-0/93	0/19	0/005	-1/3	-0/5



SEM microscope images from control group samples



SEM microscope images from bioglass group samples



SEM microscope images from gluma group samples

Discussion

Increased dental hypersensitivity is characterized by sharp, temporary, and short pain of the naked dentin is characterized in response to thermal stimulation, drying, touching, stimulating, or chemical agents (43-45). Dental susceptibility is one of the most common and, at the same time, the most painful dental diseases. About 8.9% to 15% of adults in the European population suffer from this disease and it is equally distributed between men and women, having a direct association with age (43). Increased dental hypersensitivity has been observed in more than 40 million people in the United States (46). Materials available for the treatment of dental hypersensitivity include nerve-affecting agents such as potassium nitrate and dentinal tubular blockers, including ions and salts such as stannous fluoride, sodium fluoride/stannous fluoride, potassium oxalate, ferrous oxide, strontium chloride, amino acids/proteins, such as glutaraldehyde, resins such as dentin sealers and methyl methacrylate (46, 47). The present study aimed at determining the effect of bioactive glass 45S5 and calcium oxalate on the dentinal tubular coating in dental hypersensitivity. In the present study, the comparison and assessment of the filling status of dentinal tubules in the three groups revealed that both gluma and bioglass substances were able to effectively and significantly fill the dentinal tubules. Hence, they can effectively reduce dental hypersensitivity. On the other hand, the results of this study showed that bioglass was more effective and significant than gluma in filling the dentinal tubules, so that in SEM images of bioglass, in several samples, nearly all dentinal tubules were closed; hence, it seems to be a more effective substance in reducing dental hypersensitivity.

In this study, calcium oxalate (gluma) and bioglass 45S5 (the newest bioglass produced by the knowledge-based method) was used. The reason for selecting them is that calcium oxalate is one of the most commonly used antiallergic substances extensively used in toothpaste, and bioglass has been used since today, dentistry and medicine increasingly use biologic agents (biocompatible). In their study, Felton et al. recognized that gluma had no significant effect on dental hypersensitivity decrease compared to the control group, and therefore their results revealed that gluma had no significant effect on dental hypersensitivity (48). This finding was not in line with the results of the present study. However, Schupbach et al. found that the use of gluma could effectively decrease dental hypersensitivity that is consistent with our study. Bergenholtz et al. also proved the positive effect of gluma on dental coating and decreased dental hypersensitivity in their study (49). Furthermore, in the study of Ishihata et al., gluma had a significant effect on the tooth surface coating (50). Hence, most existing studies agree with the result of the present study confirming the effectiveness of the gluma in reducing dental hypersensitivity. The mechanism of this effect is on the filling of dentinal tubules and coating the tooth surface, mentioned in the findings of the above studies.

Concerning bioglass (bioactive glass), researchers believe that if the release of silicon, calcium, and phosphorus elements is within a certain range, the bioglass is able to activate genes, inducing osteogenic differentiation of bone cells and stimulating tissue formation (51). The performance and positive effects of some of these rare elements on the metabolism and bone tissue activity are such that some researchers have tended to use the single and separate use of these elements in bone defect restoration. For instance, in a recent study, the positive effect of strontium on bone tissue growth and repair has been proven in INVIVO tests (52). The duty and function of all rare elements in bone metabolism are available in the documentation (53). Since bioglass is a foreign agent different from the host bone, it does not initially receive an appropriate response from the immune system. In other words, there is no tendency by bone cells and intermediate proteins to be absorbed into bioglass (54). Again, on the other hand, bioglass will significantly contribute to the growth and activity of bone cells and repair bone lesion in host bone through releasing calcium and phosphorus ions in the surrounding environment (55). Bioglass is known as a biomarker with high

ability of bone formation induction and it has a different bioactive mechanism from other bio-ceramics similar to it (56). Given the above, it can be concluded that bioglass is the factor for movement and absorption of cells towards the implant and an effective factor in the growth, activity and proliferation of cells. Consequently, the biofunction of this mixture (bioglass) is a combination of the best conductivity and bone induction, and its performance will be higher than the biological performance of each of all its components. Due to their weak mechanical specifications, bioglasses have many limitations in under load positions in the body (such as the occlusal surface of the teeth). Furthermore, the adhesion of bioactive glasses (bioglass) to the ground is low and they are resolved in the body over time. Accordingly, bioactive glasses are often prepared and used along with another solid material (57, 58).

In addition to the above studies, several researches have emphasized the effectiveness of the use of bioglasses in bone repair and restoration, as well as its strength enhancement. In the study of Vano et al., the addition of bioglass to toothpaste and mouthwash caused the blockage of dentinal tubules and reduced dental hypersensitivity (59). Moreover, the findings of the present study were in line with the results of the study by Hill et al. in 2015 who compared the ability of mouthwashes containing Nano-hydroxyapatite in closing the dentinal tubules compared to some commonly used anti-sensory mouthwashes (60). Xia et al. also studied the effect of bioactive particles on the treatment of dentinal hypersensitivity. In their study, the paste containing substitutive bioactive strontium particles of calcium phosphate was used on the parts prepared from the pulled molars compared to the paste containing bioactive particles-free carboxymethyl cellulose as the control group. Their study revealed that after three days of brushing with a paste containing bioactive particles, some of the tubules were blocked, and after seven days, the surface of the tubules was completely covered by an apatite layer that is in line with our study, although we did not have the possibility of analyzing ourselves at different times (61). Moreover, the positive results of using bioglass in reducing dental hypersensitivities were found in the results of Wang et al. (62), Jung et al. (63), Välimaa et al. (64), Gillam et al. (65), Tirapelli et al. (66), Wang et al. (67), Zhong et al. (68), Wang et al. (69), Litkowski et al. (70), Sauro et al. (71), Farmakis et al. (72), West et al. (73) Ma et al. (74), Bakry et al. (75), Jena et al. (76) and Mitchell et al. (77). Furthermore, the positive effect of bioactive glass 45S5 studied in this study has been confirmed and emphasized in the reduction of dental hypersensitivity in recent and valid studies and all of them have confirmed the results of this study. Among them, we can refer to the studies of Bakry et al. (78), Jones et al (79), Deng et al. (80), Bakry et al. (81), and Mehrvarzfar et al. in Iran (82). Thus, most existing studies also emphasize the role of bioglasses, in particular in dental hypersensitivity reduction, and they believe that the mechanism of the effect of these materials is the remineralization, tubular filling, and tooth and dentin surface coatings. Hence, they can be used as an effective substance to reduce dental hypersensitivity in toothpastes, saliva gel, and mouthwashes (69, 70, 73, 76). In addition to the above, some studies also emphasize the antimicrobial and, consequently, anti-decay specifications of bioglasses. Among them the study by Jung et al. (83) may be referred to.

According to the results of this study, given that the mean calcium oxalate score in Hulsman analysis is 1.9, it is estimated that oxalate is not able to block more than 50% of dentinal tubules, and this conclusion is in line with the findings of different studies on the treatment of patients with calcium oxalate, so that after the treatment of patients with gluma, their hypersensitivity is usually reduced to a small extent, and their pain relapses over time. This may be because the effect of the gluma is only mechanical, while bioglass bioactively penetrates inside the dentinal tubules and stimulate the dentin-formation. This statement of us is in line with the results of the study by Xia et al., indicating that the bioglass effect is increased over time and this can be a reason for the significant difference between bioglass and calcium oxalate (61).

Conclusion

According to our results, both bioglass and gluma substances had a significant effect on the rate of filling of the dentinal tubules compared to the control group, and there was a significant difference between the bioglass and the gluma so that the bioglass blocks more dentinal tubules.

Recommendations

Based on the results of the statistical studies, both bioglass and gluma lead to effective filling of dentinal tubules; therefore, they showed a significant decrease in hypersensitivity. Nevertheless, the bioglass has exhibited more ability in the closure of dentinal tubules and it was more effective. Hence, these compounds may be used in toothpaste and mouthwashes to reduce dental hypersensitivity. It seems that the use of bioglass combination can

increase the micro-hardness and remineralization of the teeth. Meanwhile, there are concerns about the formation of hypoplastic spots after excessive consuming or swallowing the fluoride-containing toothpaste. Hence, the use of bioglass or gluma for the prevention of dental caries in children and adults seems to be a good recommendation and address the existing concerns about hypoplastic spots and other complications. It is recommended to carry out this project in vivo on patients and assess the long-term durability of the treatment. It is also recommended to use bioglass as the antiallergenic substance to substitute the dentin-bonding agents under composite restorations.

References

- [1] Bartold P. Dentinal hypersensitivity: a review. *Australian dental journal*. 2006;51(3):212-8.
- [2] Asnaashari M, Moeini M. Effectiveness of lasers in the treatment of dentin hypersensitivity. *Journal of lasers in medical sciences*. 2013;4(1):1.
- [3] West N, Lussi A, Seong J, Hellwig E. Dentin hypersensitivity: pain mechanisms and aetiology of exposed cervical dentin. *Clinical oral investigations*. 2013;17(1):9-19.
- [4] Hashim NT, Gasmalla BG, Sabahelkheir AH, Awooda AM. Effect of the clinical application of the diode laser (810 nm) in the treatment of dentine hypersensitivity. *BMC research notes*. 2014;7(1):31.
- [5] Ranjan R, Yadwad KJ, Patil SR, Mahantesha S, Rahman AA, Bhatia VB. Efficacy of 980 nm diode laser as an adjunct to Snf 2 in the management of dentinal hypersensitivity: A controlled, prospective clinical study. *Journal of Dental Lasers*. 2013;7(2):66.
- [6] Umberto R, Claudia R, Gaspare P, Gianluca T, Alessandro DV. Treatment of dentine hypersensitivity by diode laser: a clinical study. *International journal of dentistry*. 2012;2012.
- [7] Kehua Q, Yingying F, Hong S, Menghong W, Deyu H, Xu F. A cross-sectional study of dentine hypersensitivity in China. *International dental journal*. 2009;59(6):376-80.
- [8] Chabanski M, Gillam D, Bulman J, Newman H. Prevalence of cervical dentine sensitivity in a population of patients referred to a specialist Periodontology Department. *Journal of clinical periodontology*. 1996;23(11):989-92.
- [9] Splieth CH, Tachou A. Epidemiology of dentin hypersensitivity. *Clinical oral investigations*. 2013;17(1):3-8.
- [10] Taani SQ, Awartani F. Clinical evaluation of cervical dentin sensitivity (CDS) in patients attending general dental clinics (GDC) and periodontal specialty clinics (PSC). *Journal of clinical periodontology*. 2002;29(2):118-22.
- [11] Gillam D, Seo H, Newman H, Bulman J. Comparison of dentine hypersensitivity in selected occidental and oriental populations. *Journal of oral rehabilitation*. 2001;28(1):20-5.
- [12] Kawasaki A, Ishikawa K, Suge T, Shimizu H, Suzuki K, Matsuo T, et al. Effects of plaque control on the patency and occlusion of dentine tubules in situ. *Journal of oral rehabilitation*. 2001;28(5):439-49.
- [13] Liu Y, Gao J, Gao Y, Xu S, Zhan X, Wu B. In vitro study of dentin hypersensitivity treated by 980nm diode laser. *Journal of lasers in medical sciences*. 2013;4(3):111.
- [14] Ananthakrishna S, Raghu TN, Koshy S, Kumar N. Clinical evaluation of the efficacy of bioactive glass and strontium chloride for treatment of dentinal hypersensitivity. *Journal of Interdisciplinary Dentistry*. 2012;2(2):92.
- [15] Al-Azzawi LM, Dayem RN. A comparison between the occluding effects of the Nd: YAG laser and the desensitising agent sensodyne on permeation through exposed dentinal tubules of endodontically treated teeth: an in vitro study. *Archives of oral biology*. 2006;51(7):535-40.
- [16] Glauche CE, de Freitas PM, Vieira Jr ND, Lage Marques JL. Qualitative microanalysis of ions and ultrastructural changes in dentin exposed to laser irradiation and to metal salts solution. *Lasers in Surgery and Medicine: The Official Journal of the American Society for Laser Medicine and Surgery*. 2005;36(4):334-9.

- [17] Davies M, Paice EM, Jones SB, Leary S, Curtis AR, West NX. Efficacy of desensitizing dentifrices to occlude dentinal tubules. *European journal of oral sciences*. 2011;119(6):497-503.
- [18] Hargreaves KM, Berman LH. *Cohen's pathways of the pulp expert consult*: Elsevier Health Sciences; 2015.
- [19] Schmidlin PR, Sahrman P. Current management of dentin hypersensitivity. *Clinical Oral Investigations*. 2013;17(1.9-55:)
- [20] Porto IC, Andrade AK, Montes MA. Diagnosis and treatment of dentinal hypersensitivity. *Journal of oral science*. 2009;51(3):323-32.
- [21] Lopes AO, Aranha ACC. Comparative evaluation of the effects of Nd: YAG laser and a desensitizer agent on the treatment of dentin hypersensitivity: a clinical study. *Photomedicine and laser surgery*. 2013;31(3):132-8.
- [22] Gillam DG, Chesters RK, Attrill DC, Brunton P, Slater M, Strand P, et al. Dentine hypersensitivity—guidelines for the management of a common oral health problem. *Dental update*. 2013;40(7):514-24. .
- [23] Orchardson R, Gillam DG. Managing dentin hypersensitivity. *The Journal of the American Dental Association*. 2006;137(7):990-8.
- [24] Ipci SD, Cakar G, Kuru B, Yilmaz S. Clinical evaluation of lasers and sodium fluoride gel in the treatment of dentine hypersensitivity. *Photomedicine and laser surgery*. 2009;27(1):85-91.
- [25] Cummins D. Recent advances in dentin hypersensitivity: clinically proven treatments for instant and lasting sensitivity relief. *American Journal of Dentistry*. 2010;23(A):3A-13A.
- [26] Jalalian E, Meraji N, Mirzaei M. Comparison between Two Desensitizer Materials: Potassium Nitrate and Gluma Desensitizer in Reducing Tooth Sensitivity. *Journal of Dentistry*. 2006;7(1, 2):23-34.
- [27] Pamir T, Özyazici M, Baloglu E, Önal B. The efficacy of three desensitizing agents in treatment of dentine hypersensitivity. *Journal of clinical pharmacy and therapeutics*. 2005;30(1):73-6.
- [28] Frechoso SC, Menéndez M, Guisasola C, Arregui I, Tejerina JM, Sicilia A .Evaluation of the efficacy of two potassium nitrate bioadhesive gels (5% and 10%) in the treatment of dentine hypersensitivity. A randomised clinical trial. *Journal of clinical periodontology*. 2003;30(4):315-20.
- [29] Lockard MW. A retrospective study of pulpal response in vital adult teeth prepared for complete coverage restorations at ultrahigh speed using only air coolant. *The Journal of prosthetic dentistry*. 2002;88(5):473-8.
- [30] Pereira JC, Martineli AC, Tung MS. Replica of Human Dentin Surfaces Treated With Different Desensitizing Agents: A Methodological SEM Study in Vitro. 2016.
- [31] Jalalian E, Meraji N, Mirzaei M. A comparison of the efficacy of potassium nitrate and gluma desensitizer in the reduction of hypersensitivity in teeth with full-crown preparations. *J Contemp Dent Pract*. 2009;10(1):66-73.
- [32] Hench LL. The story of Bioglass®. *Journal of Materials Science: Materials in Medicine*. 2006;17(11):967-78.
- [33] Hench L, Ethridge E. *Biomaterials, an Interfacial Approach, Biophysics and Bioengineering Series Vol. 4*. Academic Press, New York; 1982.
- [34] Rey C, Combes C, Drouet C, Lebugle A, Sfihi H, Barroug A. Nanocrystalline apatites in biological systems: characterisation, structure and properties. *Materialwissenschaft und Werkstofftechnik: Entwicklung, Fertigung, Prüfung, Eigenschaften und Anwendung gentechnischer Werkstoffe*. 2007;38(12):996-1002.
- [35] Masai H, Takahashi Y, Fujiwara T. *Glass-Ceramics Containing Nano-Crystallites of Oxide Semiconductor*. Ceramic Materials: IntechOpen; 2010.
- [36] Moreno EC, Kresak M, Zahradnik RT. Fluoridated hydroxyapatite solubility and caries formation. *Nature*. 1974;247(5435):64.
- [37] Aoba T. The effect of fluoride on apatite structure and growth. *Critical Reviews in Oral Biology & Medicine*. 1997;8(2):136-53.

- [38] Kim HW, Li LH, Koh YH, Knowles JC, Kim HE. Sol-Gel Preparation and Properties of FluorideSubstituted Hydroxyapatite Powders. *Journal of the American Ceramic Society*. 2004;87(10):1939-44.
- [39] Bianco A, Cacciotti I, Lombardi M, Montanaro L, Bemporad E, Sebastiani M. F-substituted hydroxyapatite nanopowders: thermal stability, sintering behaviour and mechanical properties. *Ceramics international*. 2010;36(1):313-22.
- [40] Brauer DS, Karpukhina N, O'Donnell MD, Law RV, Hill RG. Fluoride-containing bioactive glasses: effect of glass design and structure on degradation, pH and apatite formation in simulated body fluid. *ActaBiomaterialia*. 2010;6(8):3275-82.
- [41] Holand W, Beall GH. *Glass ceramic technology*: John Wiley & Sons; 2012.
- [42] De Aza P, De Aza A, Pena P, De Aza S. Bioactive glasses and glass-ceramics. *Boletin-Sociedad Espanola De Ceramica Y Vidrio*. 2007;46(2):45.
- [43] Li R, Clark A, Hench L. An investigation of bioactive glass powders by sol-gel processing. *Journal of Applied Biomaterials*. 1991;2(4):231-9.
- [44] Arcos D, Vallet-Regí M. Sol-gel silica-based biomaterials and bone tissue regeneration. *Actabiomaterialia*. 2010;6(8):2874-88.
- [45] Vallet-Regí M, Salinas AJ. Sol-Gel Silica-Based Biomaterials and Bone Tissue Regeneration. *Handbook of Sol-Gel Science and Technology: Processing, Characterization and Applications*. 2018:3597618.
- [46] Brinker CJ, Scherer GW. The physics and chemistry of sol-gel processing. *Sol-Gel Science*. 1989;3:115-9.
- [47] Prajatelista E, Ju SW, Sanandiya ND, Jun SH, Ahn JS, Hwang DS. Dentin Hypersensitivity: Tunicate-Inspired Gallic Acid/Metal Ion Complex for Instant and Efficient Treatment of Dentin Hypersensitivity (*Adv. Healthcare Mater.* 8/2016). *Advanced healthcare materials*. 2016;5(8):988.-
- [48] Felton DA, Bergenholtz G, Kanoy B. Evaluation of the desensitizing effect of Gluma Dentin Bond on teeth prepared for complete-coverage restorations. *International Journal of Prosthodontics*. 1991;4(3): 292-298.
- [49] Bergenholtz G, Jontell M, Tuttle A, Knutsson G. Inhibition of serum albumin flux across exposed dentine following conditioning with GLUMA primer, glutaraldehyde or potassium oxalates. *Journal of Dentistry*. 1993;21(4):220-7.
- [50] Ishihata H, Finger WJ, Kanehira M, Shimauchi H, Komatsu M. In vitro dentin permeability after application of Gluma @desensitizer as aqueous solution or aqueous fumed silica dispersion. *Journal of Applied Oral Science*. 2011;19(2):147-53.
- [51] Hench LL. Genetic design of bioactive glass. *Journal of the European Ceramic Society*. 2009;29(7):1257-65.
- [52] Tian M, Chen F, Song W, Song Y, Chen Y, Wan C, et al. In vivo study of porous strontium-doped calcium polyphosphate scaffolds for bone substitute applications. *Journal of Materials Science: Materials in Medicine*. 2009;20(7):1505-12.
- [53] Sandström B, Walter P. Role of Trace Elements for Health Promotion and Disease Prevention: Proceedings of the 1996 Annual Meeting of the European Academy of Nutritional Sciences, Copenhagen, August 22-24, 1996: Karger Medical and Scientific Publishers; 1998.
- [54] Hench LL, Polak JM. Third-generation biomedical materials. *Science*. 2002;295(5557):1014-7.
- [55] Hench L, Polak J, Buttery L, Xynos I, Maroethynaden J. Use of bioactive glass compositions to stimulate osteoblast production. *Google Patents*; 2004.
- [56] Lohbauer U, Jell G, Saravanapavan P, Jones JR, Hench LL, editors. Indirect cytotoxicity evaluation of silver doped bioglass Ag-S70C30 on human primary keratinocytes. *Key Engineering Materials*; 2005: Trans Tech Publ. Vol. 284, pp. 431-434.
- [57] Muhonen V, Kujala S, Vuotikka A, Ääritalo V, Peltola T, Areva S, et al. Biocompatibility of sol-gelderivedtitania-silica coated intramedullary NiTi nails. *ActaBiomaterialia*. 2009;5(2):785-93.

- [58] Ääritalo V, Areva S, Jokinen M, Lindén M, Peltola T. Sol-gel-derived TiO₂-SiO₂ implant coatings for direct tissue attachment .Part I: design, preparation and characterization. *Journal of Materials Science: Materials in Medicine*. 2007;18(9):1863-73.
- [59] Vano M, Derchi G, Barone A, Covani U. Effectiveness of nano-hydroxyapatite toothpaste in reducing dentin hypersensitivity: A double-blind randomized controlled trial. *Quintessence international*. 2014;45(8):703-11.
- [60] Hill RG, Chen X, Gillam DG. In vitro ability of a novel nanohydroxyapatite oral rinse to occlude dentine tubules. *International journal of dentistry*. 2015;2015.
- [61] Xia W ,Qin T, Suska F, Engqvist Hk. Bioactive spheres: the way of treating dentin hypersensitivity. *ACS Biomaterials Science & Engineering*. 2016;2(5):734-40.
- [62] Wang Y-L, Chiang Y-C, Chang H-H, Lin H-P, Lin C-P. Novel calcium encapsulated mesocellular siliceous foams for crystal growth in dentinal tubules. *Journal of dentistry*. 2019;83:61-6.
- [63] Jung J-H, Park S-B, Yoo K-H, Yoon S-Y, Bae M-K, Lee DJ, et al. Effect of different sizes of bioactive glass-coated mesoporous silica nanoparticles on dentinal tubule occlusion and mineralization. *Clinical oral investigations*. 2019;23(5):2129-41.
- [64] Välimaa S, Perea-Lowery L, Smått J-H, Peltonen J, Budde T, Vallittu P. Grit blasted aggregates of hydroxyl apatite functionalized calcium carbonate in occluding dentinal tubules. *Heliyon*. 2018;4(12):e01049.
- [65] Gillam D, Tang J, Mordan N, Newman H. The effects of a novel Bioglass® dentifrice on dentine sensitivity: a scanning electron microscopy investigation. *Journal of Oral Rehabilitation*. 2002;29(4):30513.
- [66] Tirapelli C, Panzeri H, Soares RG, Peitl O, Zanutto ED. A novel bioactive glass-ceramic for treating dentin hypersensitivity. *Brazilian oral research*. 2010;24(4):381-7.
- [67] Wang Z, Jiang T, Sauro S, Pashley DH, Toledano M, Osorio R, et al. The dentine remineralization activity of a desensitizing bioactive glass-containing toothpaste: an in vitro study. *Australian Dental Journal*. 2011;56(4):372-81.
- [68] Zhong Y, Liu J, Li X, Yin W, He T, Hu D, et al. Effect of a novel bioactive glass-ceramic on dentinal tubule occlusion: an in vitro study. *Australian dental journal*. 2015;60(1):96-103.
- [69] Wang Z, Sa Y, Sauro S, Chen H, Xing W, Ma X, et al. Effect of desensitising toothpastes on dentinal tubule occlusion: a dentine permeability measurement and SEM in vitro study. *Journal of Dentistry*. 2010;38(5):400-10.
- [70] Litkowski LJ, Hack GD, Greenspan DC. Compositions containing bioactive glass and their use in treating tooth hypersensitivity. *Google Patents*; 2002.
- [71] Sauro S, Watson TF, Thompson I. Dentine desensitization induced by prophylactic and airpolishing procedures: an in vitro dentine permeability and confocal microscopy study. *Journal of dentistry*. 2010;38(5):411-22.
- [72] Farmakis E-TR, Beer F, Kozyrakakis K, Pantazis N, Moritz A. The influence of different power settings of Nd: YAG laser irradiation, bioglass and combination to the occlusion of dentinal tubules. *Photomedicine and laser surgery*. 2013;31(2):54-8.
- [73] West N, Addy M, Hughes J. Dentine hypersensitivity: the effects of brushing desensitizing toothpastes, their solid and liquid phases, and detergents on dentine and acrylic: studies in vitro. *Journal of oral rehabilitation*. 1998;25(12):885-95.
- [74] Ma Q, Wang T, Meng Q, Xu X, Wu H, Xu D, et al. Comparison of in vitro dentinal tubule occluding efficacy of two different methods using a nano-scaled bioactive glass-containing desensitising agent. *Journal of dentistry*. 2017;60:63-9.
- [75] Bakry AS, Al-Hadeethi Y, Razvi MAN. The durability of a hydroxyapatite paste used in decreasing the permeability of hypersensitive dentin. *Journal of dentistry*. 2016;51:1-7.

- [76]Jena A, Kala S, Shashirekha G. Comparing the effectiveness of four desensitizing toothpastes on dentinal tubule occlusion: A scanning electron microscope analysis. *Journal of conservative dentistry: JCD*. 201.269;)4(20;7
- [77]Mitchell JC, Musanje L, Ferracane JL. Biomimetic dentin desensitizer based on nano-structured bioactive glass. *Dental Materials*. 2011;27(4):386-93.
- [78]Bakry A, Takahashi H, Otsuki M, Sadr A, Yamashita K, Tagami J. CO2 laser improves 45S5 bioglass interaction with dentin. *Journal of dental research*. 2011;90(2):246-50.
- [79]Jones JR, Brauer DS, Hupa L, Greenspan DC. Bioglass and bioactive glasses and their impact on healthcare. *International Journal of Applied Glass Science*. 2016;7(4):423-3.4
- [80]Deng M, Wen H-L, Dong X-L, Li F, Xu X, Li H, et al. Effects of 45S5 bioglass on surface properties of dental enamel subjected to 35% hydrogen peroxide. *International journal of oral science*. 2013;5(2):103.
- [81]Bakry A, Takahashi H, Otsuki M, Tagami J. The durability of phosphoric acid promoted bioglass– dentin interaction layer. *Dental Materials*. 2013;29(4):357-64.
- [82]Mehrvarzfar P, Akhavan H, Rastgarian H, Akhlagi NM, Soleymanpour R, Ahmadi A. An in vitro comparative study on the antimicrobial effects of bioglass 45S5 vs. calcium hydroxide on *Enterococcus faecalis*. *Iranian endodontic journal*. 2011;6(1):29.
- [83]Jung J-H, Kim D-H, Yoo K-H, Yoon S-Y, Kim Y, Bae M-K, et al. Dentin sealing and antibacterial effects of silver-doped bioactive glass/mesoporous silica nanocomposite: an in vitro study. *Clinical oral investigations*. 2019;23(1):253-66.