Current Usage of Glutaraldehyde/HEMA

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The use of glutaraldehyde/2-hydroxyethylmethacrylate (HEMA) combinations has been recommended for routine use in restorative dentistry by many authors and opinion leaders. Clinical restorative sites are colonized by bacteria that can contribute to postoperative sensitivity or recurrent caries. The structure of dentin allows for fluid conductance, which has been identified by Brännström as the cause of dentin sensitivity and as well, its water content challenges short- and long-term adhesion.
The glutaraldehyde/HEMA combination is stated to be antimicrobial, a flocculating agent that strengthens collagen, and an agent that can create tubular occlusion, thereby reducing postoperative sensitivity by limiting fluid movement without affecting the strength of bonding or adhesive cements. This Critical Appraisal reviews five publications that deal with the various issues and clinical challenges described above, and provides suggestions for additional reading. A Bottom Line summary is provided.

Growth of Bacterial Organisms

In Vitro Inhibition of Bacterial Growth Using Different Dental Adhesive Systems

R. WALTER, W.R. DUARTE, P.N.R. PEREIRA, H.O. HEYMANN, E.J. SWIFT, R.R. ARNOLD
Operative Dentistry 2007 (32:388–93)

ABSTRACT

Objectives: This study evaluated the antibacterial potential of four different adhesive systems.

Materials and Methods: The adhesives used in this study were Gluma Comfort Bond + Desensitizer (Heraeus Kulzer, Hanau Germany), Gluma Comfort Bond (Heraeus Kulzer), both of which are etch-and-rinse adhesives, and iBond (Heraeus Kulzer) and One-Up Bond F (Tokuyama, Tokyo, Japan), which are self-etching adhesives. Glutaraldehyde is present in Gluma Comfort Bond + Desensitizer and iBond. The bonding systems were applied to 6.5-mm paper discs, the solvents were evaporated, and the adhesives were light-activated for 20 seconds using a halogen curing unit.

Four species of bacteria were tested: *Streptococcus mutans*, *Streptococcus sobrinus*, *Lactobacillus acidophilus*, and *Actinomyces viscosus*. The bacteria were cultured, and suspensions were prepared and placed on agar plates. The specimens were placed on the freshly inoculated agar plates for initial values and then were tested at 1 week, 1 month, 3 months, and 6 months of storage. Each plate contained five discs, one

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of each adhesive group plus a blank disc. The zone of bacterial inhibition of growth was measured using callipers.

Bactericidal activity was tested with measured cultures of the bacteria placed on the surface of the cured adhesive discs or a blank disc. The bacteria were recovered after 1 hour, and the number of recovered viable bacterial determined by counting colonies of dilutions. A 100-fold reduction in recoverable CFU/mL compared with the blank disc was interpreted as significant killing.

Results: The bacterial assays showed that all of the tested materials were capable of killing the test strains at the initial time. All of the materials inhibited development of bacterial growth immediately under the disk even when aged to 6 months. The inhibition of bacterial growth noted with iBond, especially against mutans streptococci, tended to be greater than the others.

Conclusions: The assays revealed potentially important differences in antimicrobial properties of distinct formulations of dental adhesives. The tested materials had a potential effect against representative oral plaque bacteria with cariogenic potential. This effect was demonstrated to be long-lasting in the in vitro simulation. iBond (which contains 4-META, UDMA, glutaraldehyde, acetone, and water) was the only adhesive system tested that was able to kill all the bacteria through at least 1 week of aging.

COMMENTARY

This study shows that when glutaraldehyde is included in the adhesive formulation, it has the potential to demonstrate an immediate and long-term antimicrobial effect. This evidence, that it is bactericidal and bacteriostatic when combined with an adhesive, is noteworthy. Multiple studies show that when glutaraldehyde is used as a separate entity before the bonding procedure, long-term antibacterial effects can also be demonstrated. Considering that microleakage and marginal gaps are present in a large proportion of composite restorations and cements, this long-term antimicrobial effect could prevent bacterial growth in these areas, minimizing the potential for secondary caries. It is also significant to note that the antimicrobial effect of glutaraldehyde on dentin has been shown to be dramatically higher on dentin than on the agar plates used in this study.

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Effects on Collagen

Changes in Stiffness of Demineralized Dentin Following Application of Collagen Cross-linkers

A.K. BEDRAN-RUSSO, D.H. PASHLEY, K. AGEE, J.L. DRUMMOND, K.J. MIESCKE

Journal of Biomedical Materials Research Part B: Applied Biomaterials 2008 (86B:330–4)

ABSTRACT

Objectives: The purpose of the study was to evaluate the effect of two collagen cross-linking agents, glutaraldehyde and grape seed extract (GSE), on the modulus of elasticity of demineralized dentin, when used at different concentrations and exposure times. Type I collagen provides tissues and organs with tensile strength, form, and cohesiveness. It is thought that increasing the strength of the dentin matrix using cross-linking agents might improve both the strength and the durability of resin-dentin bonds.

Materials and Methods: Sound extracted molar teeth were ground flat and the teeth were sectioned into 0.5-mm beams and trimmed with a bur to create rectangular blocks of dentin. These were etched with 10% phosphoric acid for 5 hours to cause complete tissue demineralization. They were then treated with 2.5%, 5%, or 25% glutaraldehyde (Fisher Biotech, Fair Lawn, NJ) and 0.65% or 6.5% grape seed extract Mega-Natural (Polyphenolics, Madera, CA). The specimens were immersed in water for baseline measurements and then in their respective solutions for 10 minutes, 30 minutes, 1 hour, 2 hours, and 4 hours of cumulative exposure. Modulus of elasticity was measured using a three-point bend method. A total of 10 to 12 specimens were evaluated per group.

Results: The mean baseline modulus of elasticity (E) values varied between 4.8 and 6.2 MPa in water. After 4 hours of treatment, the values increased up to 34.9 and 242.5 MPa, depending on treatment time and cross-linking agent. The 25% glutaraldehyde resulted in a significantly more rapid rise in E after 10 minutes than 2.5% and 5%, and the use of 0.65% and 6.5% GSE resulted in a statistically significant increase in the E of demineralized dentin following each time tested, with 6.5% GSE being the highest. A statistically significant interaction was observed between the factors studied (treatment and time).

Conclusions: Demineralized dentin stiffness is affected by the use of glutaraldehyde and grape seed extract collagen cross-linking agents. The changes to the dentin matrix after treatment with the cross-linkers were both concentration and time dependent.

COMMENTARY

Increasing the strength of the dentin matrix with cross-linkers may improve both the strength and the durability of resin-dentin bonds. 2-hydroxyethylmethacrylate (HEMA) can react with dentin collagen due to its ester group and its hydroxyl group with collagen because of its hydrophilic nature. Glutaraldehyde/HEMA products also contain water so they react as wetting agents to expand the demineralized collagen and increase its surface energy, which also might create higher and more durable bonds.

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Tubular Structure and Dentin Hypersensitivity

Spectroscopic Investigation of the Function of Aqueous 2-Hydroxyethylmethacrylate/Glutaraldehyde Solution as a Dentin Desensitizer

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European Journal of Oral Sciences 2006 (114:354–9)

ABSTRACT

Objectives: Fourier-transform (FT)-Raman and infrared (IR) spectroscopy were employed to investigate the function of the aqueous 2-hydroxyethylmethacrylate (HEMA)/glutaraldehyde (GA) solution (Gluma) as a desensitizer.

Materials and Methods: HEMA, GA, and the mixture of HEMA + GA were used to interact with dentin, collagen, hydroxyapatite (HAP), and bovine serum albumin (BSA) individually. To look at dentin, freshly extracted molars were sectioned into 1.5-mm thick dentin slices, pretreated with 37% phosphoric acid for 30 seconds, washed, and dried. The slices were cut into four blocks which were immersed in the solutions. Then collagen and HAP were immersed as well. BSA was diluted 1:3 to simulate dentinal fluid and the materials tested with it.

Results: The FT-Raman spectrum of dentin, the interaction of GA, HEMA, and Gluma with collagen and HAP, and the interaction of GA, HEMA, and Gluma with BSA were tabulated. HEMA was shown to be absorbed onto the dentin surface and because of the hydrogen bond between HEMA and dentinal collagen, it could not be removed by washing, indicating that HEMA acts as a preprimer attaching to collagen. Collagen was cross-linked by glutaraldehyde, which strengthens the collagen fibrils. There is a compound formed when BSA is cross-linked with GA. The cross-linking of BSA by Gluma results in precipitation that occludes the dentinal tubules.

Conclusions: When Gluma is applied in vivo, two reactions occur. First, GA reacts with part of the serum albumin in dentinal fluid, which induces a precipitation of serum albumin. Second, the reaction of GA with serum albumin induces the polymerization of HEMA. The function of Gluma as a desensitizer to block dentinal tubules is completed by these two reactions.

COMMENTARY

Brännström effectively explained dentin hypersensitivity as the hydrodynamic theory of pain. Therefore, the treatment focus for this sensitivity has generally been on covering the exposed dentin with an impermeable layer to prevent the osmotic gradient. However, some of the surface precipitants, like some oxalates, can affect and decrease the resultant final bond strength. Glutaraldehyde as an effective fixative or flocculating agent can create a coagulation plug inside the dentinal tubules, thus readily reducing or totally eliminating tooth sensitivity. This precipitate thus would theoretically reduce the positive pressure fluid flow of the dentin, which might increase or stabilize the dentin bond long-term.

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Effects on Bonding to Tooth Structure Treated with Glutaraldehyde/HEMA

The Use of Collagen Cross-linking Agents to Enhance Dentin Bond Strength

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Journal of Biomedical Research Part B: Applied Biomaterials 2009 (91:419–24)

ABSTRACT

Objectives: Because collagen is a major component of the hybrid layer, an improvement of its mechanical properties might be advantageous during bonding procedures. This study investigated the effect of three different cross-linking agents—glutaraldehyde (GA), grape seed extract (GSE), and Genipin (GE) (Wako Pure Chemical Industries, Osaka, Japan), a Gardenia fruit extract natural cross-linker—on resin-dentin tensile bond strengths (TBS).

Materials and Methods: Sixty-four sound human molars were collected and their occlusal surfaces were ground flat to expose dentin. The dentin surfaces were etched using 35 to 37% phosphoric acid for 15 seconds, rinsed and kept moist. Cross-linking agents were applied to the etched dentin (5% GA, 6.5% GSE, and 0.5% GE at a pH of 7.4), with phosphate buffer used as a control. The teeth were restored using either acetone-based One-Step Plus (Bisco, Inc., Schaumburg, IL) or ethanol-based Adper Single Bond Plus (3 M ESPE, St. Paul, MN) adhesive systems and a composite material in 2-mm increments to a total height of 5 mm to allow for gripping during tensile testing. After 24 hours of storage in distilled water, specimens were sectioned to produce a cross-sectional surface area of 1.0 mm^2 and were tested for tensile bond strength. The debonded surfaces were classified as adhesive failure at the interface, cohesive failure in the composite or in adhesive. The micromorphology of the fractured interface was assessed using scanning electron microscopy.

Results: For Adper Single Bond, two of the cross-linking agents significantly increased mean TBS. There was an increase of more than double for the control, from 33.38 to 68.96 MPa for GA and 71.06 for GSE. Results were similar for One-Step Plus. Bond strengths increased from the control of 44.13 to 65.46 MPa for the GA treatment and 74.40 MPa for GSE. There was no statistically significant difference with the GE-treated samples. The mode of fracture at the interface showed that a majority were at the interface; however, the GSE and GA samples showed a distinct difference, with the fracture being at the top of the hybrid layer with a morphology showing that the bond had undergone excessive strain and plastic deformation.

Conclusions: The chemical modification to the dentin matrix promoted by GA and GSE, but not GE, resulted in significantly increased bond strengths. The application of selective collagen cross-linkers during adhesive restorative procedures might be a new approach to improve dentin bond strengths.

COMMENTARY

As we prepare deeper into dentin, there is an increase in dentinal tubules per unit area and an increase in wetness that makes dentin bonding more difficult. There is evidence to show that blocking dentinal tubules and blocking tubular fluid can decrease dentinal adhesive deterioration. Multiple studies have shown that chemical cross-linking to etched dentin prior to bonding significantly enhances dentin bond strengths when using glutaraldehyde/2-hydroxyethylmethacrylate

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(HEMA) combinations and the mixture does not interfere with the bonding procedure whether or not acetone or alcohol primers are used. However, little information can be found in the literature about how this combination of glutaraldehyde/HEMA affects the smear layer when self-etch bonding systems are used. A small amount of HEMA added to a self-etch material might improve the strength, but some self-etch bonding systems are unaffected by glutaraldehyde/HEMA combination products used as desensitizers and antimicrobial agents. More research needs to be done in this area.

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Effect on Cementation

The Effect of Resin Desensitizing Agents on Crown Retention

E.J. SWIFT, A.H. LLOYD, D.A. FELTON

Journal of the American Dental Association 1997 (128:195–200)

ABSTRACT

Objective: This laboratory study evaluated the use of resin primers and adhesives that are used to prevent postcementation sensitivity, to see if there is any effect of these desensitizing agents on the retention of full crown restorations.

Materials and Methods: Thirty extracted human molar teeth were mounted in molds using self-cure acrylic using a surveyor to position the long axis of the crown to that of the mold. The specimens were prepared for full crown coverage using a specially designed apparatus to create standardized preparations. Each tooth was prepared with an axial wall height of 4 mm and a taper of 2.4 per wall with a 1.5 mm axial tooth reduction. Full crown patterns were waxed directly on the teeth with an attachment fabricated and full crowns were fabricated in a silver-palladium casting alloy. The castings were abraded with 50-μm aluminum oxide, tried on the teeth, and adjusted for proper fit.

Ten of the teeth were treated with One-Step, which is an etch-and-rinse one-bottle (primer + adhesive) bonding agent and 10 with Gluma Desensitizer; the remaining 10 were left as untreated controls. The crowns were cemented with zinc phosphate cement and stored for 24 hours in water at room temperature.

The castings were placed on a universal testing machine in such a manner as to be parallel with the directional axis of draw. With a crosshead speed of 0.5 mm/minute, a tensile force was applied to the casting until the cement failed and the load at failure was recorded in Newtons.

The crowns and teeth were cleaned and the surfaces were lightly roughened with the surfaces retreated as above. This process was repeated with an encapsulated conventional glass ionomer luting cement (Fuji I, GC America, Alsip, IL) and then with a resin-modified glass ionomer cement (Vitremer Luting Cement, 3 M ESPE).

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Results: The crowns cemented with the conventional glass ionomer and resin-modified glass ionomer cement had significantly higher retention values than those cemented with zinc phosphate cement. There was no statistically significant difference for the retention with or without the desensitization step.

Conclusion: This study demonstrates that the use of a resin primer or an adhesive system has no effect on the retentive properties of three different types of luting cement.

COMMENTARY

This study showed that there is no difference in retention of cemented crowns when using zinc phosphate, glass ionomer, or resin-modified glass ionomer cements preceded by application of a primer or adhesive. Other studies have shown no effect on crown retention for the same categories of cements from other manufacturers. Numerous studies show that the use of glutaraldehyde/HEMA desensitization/disinfection with adhesively cemented crowns has little effect on retention and may in fact increase retention with some resin cements.

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THE BOTTOM LINE

Numerous glutaraldehyde/HEMA products are available, including G5 (Clinician's Choice, New Milford, DT), Microprime G (Danville Materials, Danville, CA), Hema-Glu Desensitizer G (Health Dent'l, Naperville, IL), Alpha-Ease (Dental Technologies, Inc., Lincolnwood, IL), Glu/Sense (Centrix, Shelton, CT), Gluma (Heraeus Kulzer), Hemaseal-G (Germiphene, Brantford, ON, Canada), and Calm It (Dentsply Caulk, Milford, DE).

These glutaraldehyde/HEMA combination products can:

- Disinfect tooth preparations that are infected with oral bacteria.
- Have a residual antimicrobial effect that can mitigate recurrent caries due to microleakage caused by composite resin contraction upon polymerization.
- Act as a cross-linking agent or flocculating agent for collagen, increasing the strength and durability of resin-dentin bonds.
- Effectively block dentinal tubules with a coagulation plug, decreasing fluid flow and thereby reducing post-operative sensitivity.
- Increase or enhance dentin bond strengths when using acetone- or alcohol-based etch-and-rinse bonding systems.
- Possibly affect the bond strengths of self-etch adhesive systems, but the paucity of literature in this area warrants further research.
- Be safely used prior to the cementation of full-coverage crown restorations with zinc phosphate, glass ionomer, resin-modified glass ionomer, and adhesive resin-based cements.

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