Glutaraldehyde/HEMA in Clinical Dentistry

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LEARNING OBJECTIVES
After reading this article, the individual will learn:
• An overview of the mechanism of action of glutaraldehyde/hydroxyethyl methacrylate (HEMA) combinations on dentin, and the multiple benefits of using products containing these compounds in everyday clinical protocols.
• A summary of the current literature regarding glutaraldehyde/HEMA compounds and direction of use for these compounds.

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Disclosure: Dr. Boksman is a paid part-time consultant to Clinical Research Dental/ Clinician’s Choice with the title of Director of Clinical Affairs.

INTRODUCTION
Every day the practicing clinician is faced with treating patients restoratively and preventatively to achieve long-term clinical results, while trying to keep abreast of the best treatment modalities, options, and anticipated outcomes, based on clinical experience and the current published literature. In the area of disinfection and desensitization, much has been published; many different approaches have been suggested, with some of the literature contradictory. Work done by the TRAC Research team has shown “that 100% of preparations are highly colonized with a variety of organisms, and that water cooled cutting followed by rinsing, drying, and acid etching—with or without rubber dam isolation—did not eliminate these micro-organisms.”

In addition to the restorative site being colonized by bacteria (which may or may not facilitate recurrent caries), the inherent structure of the dentin creates a challenge when trying to effectively bond or adhere to it with long-term stability. Multiple studies have confirmed that bonding of resin to dentin shows bond degradation over time. De Munck et al and Meiers and Young have shown that for total-etch adhesives, a simplification from a 3-step application utilizing a separate primer to a 2-step application technique results in a significant decrease in tensile bond strength and shear bond strengths of the 2-step total-etch adhesive. The same study by De Munck et al states that a good surrounding resin-enamel bond protects the resin-dentin interface against water degradation.

In “A Critical Review of the Durability of Adhesion to Tooth Structure: Methods and Results,” the authors discuss the chemical and mechanical degradation of dentin resin interfaces by hydrolysis, plasticizing of the resin, bacterial enzymes, dentinal structure effects such as deproteinization of collagen, mechanical stress, temperature effects, fracture toughness of the materials, fatigue resistance, composite shrinkage resulting in microleakage and nanoleakage, effect of different solvents in the bonding materials, and technique sensitivity. The conclusions in this very excellent overview are that 3-step ethanol-water-based etch-and-rinse adhesives are still the “gold standard” in terms of bond durability, with a 2-step etch-and-rinse performing less favorably. The 2-step self-etch bonding agents demonstrated a similar trend in that long-term water storage decreases the microtensile bond strengths and the simplification to a one-step self-etching adhesive demonstrates a disappointing bonding effectiveness. De Munck et al state that “to create hydrolytic stability of cured dentin adhesives seems to rely on the application of a solvent-free, neutral pH, hydrophobic adhesive resin layer in a separate step with any simplification of the technique resulting in a loss of bonding effectiveness.”

To complicate matters even more, the clinician is faced with multiple bonding/adhesive/restorative/cementation materials choices, with some of these material combinations being incompatible with each other, resulting in zero bond strength to the dentin substrate.

This article summarizes the current status of glutaraldehyde/hydroxyethyl methacrylate (HEMA)-containing materials in restorative dentistry (Table) as found in the dental literature, and how this combination affects the
viability/growth of bacterial micro-organisms, the structure of the collagen, the tubular structure of the dentin, the postoperative sensitivity often accompanying restorative dentistry, the bonding strengths of dentin bonding agents and adhesive cements, and the effects on recurrent caries when microleakage is present.

**DISINFECTION OF TOOTH PREPARATIONS**

The carious process is initiated and progresses by the action of bacteria and their acidic byproducts. Clinically, restorative procedures are dictated by the removal of the carious material with a thorough debridement of the cavity preparation, but mechanical debridement does not eliminate the bacteria. Due not only to the bacterial process of tooth caries, but also to pulpal inflammation, recommendations have been made to use an antimicrobial cavity cleanser after tooth preparation, before tooth restoration, before the cementation of crowns, and before the placement of sealants.

One study evaluated the following disinfectant solutions: 2% chlorhexidine (Consepsis [Ultradent Products]), 2% chlorhexidine (Klorhex [Drogan]), 5.25% NaOCl, 3% H₂O₂, and their physiological saline serial dilutions (one half, one quarter, and one eighth of each), 32% phosphoric acid (Uni-Etch [Bisco]), and 32% phosphoric acid with benzalkonium chloride (BAC) (Uni-Etch BAC [Bisco]). All of the tested disinfectant solutions showed antibacterial activity against *Streptococcus mutans*. The study concluded that their use as cavity disinfectants would not be necessary when a phosphoric acid etchant alone was used. Multiple studies and articles discuss that using the acid-etch technique with dentin bonding is antimicrobial in itself, and a separate antimicrobial is not needed to kill bacteria. However, *CLINICIANS REPORT* of November 2009 claims that acid-etching does not kill the acid-producing (acidogenic), acid-loving (acidophilic) organisms active in dental caries and in fact may stimulate their activity. With the use of self-etching bonding agents (the so-called sixth- and seventh-generation bonding agents) and when using the newer self-etching cements or other cements such as resin-modified glass ionomers (RMGIs), the smear layer is incorporated into the adhesive, and thus inherent in the technique is leaving imbedded bacteria in the restorative material. Keyes described the 3 interactive necessities for caries as a susceptible host, suitable substrate, and cariogenic microflora. Mertz-Fairhurst et al have shown that when bacteria are fully sealed under restorations caries is arrested. However, most dental materials permit the microleakage of bacteria, bacterial products, and oral fluids to reach dentin, with the oral fluids then providing substrate for any residual bacteria. Direct and indirect restorations that end on areas lacking in enamel such as the cementum-dentin substrate show less stable substrate bonding, less micromechanical retention, and thus favor microleakage. What should the clinician do when the restorative technique cannot guarantee that all bacteria have been removed?

In a study published by Gharizadeh et al, the authors look
Glutaraldehyde/HEMA in Clinical Dentistry

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that restorations made in shallow and medium depth cavities demonstrate significantly less postoperative sensitivity than those made in deep cavities, which might be related to more and larger tubules, with more positive fluid flow, or to the irritating effects of the materials used. Boksmans states “it is no surprise that the accepted treatments focus on occluding the dentinal tubules, by various precipitates, or covering the exposed dentin with an impermeable layer to prevent the osmotic gradient changes that create the painful stimuli.” When oxalate desensitizers such as Super Seal (Phoenix Dental) are used to block or cover the dentinal tubules, tests showed they can reduce bond strengths significantly, and oxalate desensitizers show a low bond strength or reduced baseline bond strength when used with low pH (acidic) adhesives.

Glutaraldehyde is a very effective fixative or flocculating agent having the ability to create a coagulation plug inside the dentinal tubules. It has been accepted extremely well by dentists as a material that reduces or totally eliminates tooth sensitivity. Schüpbach and others have shown that after topical application of glutaraldehyde to the dentin surface, multiple transverse septa occurred in the lumen of the dentinal tubules down to a depth of 200 µm, effectively creating a barrier that eliminates the hydrodynamic mechanism of dentin hypersensitivity. Qin et al. showed in their study of HEMA and glutaraldehyde that a myriad of reactions occurred: HEMA was absorbed by dentin and collagen, glutaraldehyde could cross-link with collagen and serum albumin, serum albumin plus glutaraldehyde resulted in the polymerization of HEMA, and the desensitizing reaction occurs first by glutaraldehyde reacting with serum albumin in the dentinal fluid, which induces a precipitation of serum albumin, followed by a second reaction of glutaraldehyde which induces polymerization of HEMA.

Does the decrease in dentin permeability and the creation of a complex of HEMA with collagen affect bonding ability?

**EFFECTS ON BONDING TO TOOTH STRUCTURE TREATED WITH GLUTARALDEHYDE/HEMA**

In a study on dentin bonding variables that include the wetness of dentin and the presence of pulpal pressure, Perdigão states that an increase in the number of tubules with depth, and consequently an increase in dentin wetness make bonding to deeper dentin more difficult than to superficial dentin, with the outward seepage increased by acid-etching. He states that some dentin desensitizers show promise with the blocking of dentinal tubules and blocking tubular fluid which deteriorates the bonding for some current adhesives. Al-Ammar et al. found that “the application of selective collagen cross-linkers during adhesive restorative procedures may be a new approach to improve dentin bond strength properties” and showed that the chemical modification to the dentin matrix promoted by glutaraldehyde increased bond strengths using 2 fifth-generation bonding agents. Multiple studies have shown that this chemical cross-linking to etched dentin prior to bonding, significantly enhanced the dentin bond strengths with some of the highest bond strengths obtained with dentin that was rewetted with glutaraldehyde/HEMA. It has also been shown that a glutaraldehyde/HEMA solution does not interfere with the bonding procedure to dentin when either an acetone primer or an alcohol-based primer is used.

However, there is very little information or research data in the dental literature on the effect of glutaraldehyde/HEMA on the smear layer and bonding capacity of the self-etching bonding systems—the so called sixth- and seventh-generation of bonding agents. In work by Chersoni et al., when looking at fluid transudation across 4 one-step self adhesives, his team reported that fluid flow droplets could be universally identified on the surface of the bonding material, and the presence of a smear layer resulted in a decrease in conductance of dentinal fluid that was only 12% to 18% of those recorded with the acid-etch technique. Is it possible that tubule occlusion and the resultant decrease in fluid flow created after the application of glutaraldehyde/HEMA may also positively affect these generations of bonding? A small amount of HEMA when added to a self-etch bonding system seems to improve the bond strength. In a 2005 report, Lehmann and De-grange found that Clearfil SE Bond (Kuraray America) was not affected by the desensitizing agents tested, which included the glutaraldehyde/HEMA combination, and similar results have been reported by Chaconas and Burgess. More research needs to be done in this area as self-etching bonding systems are currently in wide use.
**EFFECT ON CEMENTATION**

When cementing crowns with zinc phosphate, glass ionomer, or RMGI cements, desensitization with glutaraldehyde/HEMA has little or no effect on the retention of the cemented crowns. Johnson et al\(^6\) reported that when using Mizzy zinc phosphate, Ketac-Cem glass ionomer, and resinomer, the glutaraldehyde desensitizing based system used as a desensitizing treatment for prepared teeth had no effect on crown retention for any of the 3 cements evaluated, with the modified resin cement producing the highest mean dislodgment stress that exceeded the strength of the tooth. Numerous studies show that the use of glutaraldehyde/HEMA desensitization with the placement of adhesively cemented crowns has little effect on retention, and this treatment may in fact increase retention with some resin cements.\(^7\)

**CONCLUSION**

The ability of the desensitizing agent glutaraldehyde/HEMA to effectively disinfect tooth preparations, have a postapplication antibacterial effect, act as a flocculating agent to stabilize and enhance bonding to collagen, block fluid flow in dentinal tubules, strengthen the collagen matrix, rewet the dentin to enhance acid-etch bonding, strengthen bonding with the acid-etch technique of fourth- and fifth-generation materials, have no adverse effects on cements used for crown and bridge, and have no adverse effects on adhesively luted crowns, makes this combination of materials a powerful adjunctive tool for restorative dentistry.

**REFERENCES**


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POST EXAMINATION QUESTIONS

1. The factors influencing the longevity of resin bonding to dentin can include:
   a. The action of hydrolysis and plasticizing of the resin.
   b. Bacterial enzymes and the deproteinization of collagen.
   c. Composite shrinkage and mechanical stress.
   d. All of the above.

2. Studies of bonding to tooth structure show that:
   a. The 3-step total etch acetone based bonding agents are the gold standard.
   b. The 2-step etch-and-rinse bonding agents are best.
   c. The 2-step self-etch bonding agents show decreases in strength in water storage.
   d. The one-step self-etch adhesives show good bond strengths.

3. Disinfectant solutions in restorative dentistry may be indicated because:
   a. Acid-etching of the dentin may not kill all bacteria.
   b. Self-etching adhesives leave the smear layer which is contaminated with bacteria.
   c. Self-etching cements and resin modified glass ionomers may leave residual bacteria trapped under them when used.
   d. All of the above.

4. Glutaraldehyde is a good preparation disinfectant to use because:
   a. It has a broad spectrum of activity.
   b. It does not destroy fungi and viruses.
   c. It does not affect bacterial growth on tooth/restoration interfaces.
   d. It works better on agar plates than dentin.

5. Glutaraldehyde/hydroxyethyl methacrylate (HEMA) combinations can increase the strength of the dentin matrix and thereby increase the durability of the bond by:
   a. Drying out the collagen so the fiber stands up better for adhesive penetration.
   b. Acting as a cross-linking agent to strengthen the collagen.
   c. The hydrophobic primer helps incorporation of the collagen fibrils.
   d. The water contained in these types of product may make the surface too wet and thereby decrease bond strengths.

6. Glutaraldehyde/HEMA combinations have been shown to:
   a. Decrease the moisture content of the dentin, thereby increasing bond strengths.
   b. Stop the nerve conduction of pain.
   c. Create a coagulation plug in the dentin stopping fluid flow.
   d. HEMA plays little role in the reaction of glutaraldehyde with collagen.
7. Glutaraldehyde/HEMA combinations have been shown to:
   a. Increase bond strength using fifth-generation bonding agents.
   b. Create highest bond strength on etched dentin surfaces.
   c. Have conflicting data on use with self-etching bonding agents.
   d. All of the above.

8. When cementing crowns the use of glutaraldehyde/HEMA combinations:
   a. Cannot be used with zinc phosphate, glass ionomer or resin modified cements.
   b. Cannot be used with resinomer cements.
   c. When used with modified resin cements can exceed the strength of the tooth.
   d. Can decrease the retention of adhesively cemented crowns.

9. When changing the bonding technique by combining the multiple steps into a simplified 2-step technique:
   a. The bonding strength increases over time.
   b. Since the technique is simpler and more predictable, the bond strength is the same.
   c. Tensile and shear bond strength are unaffected.
   d. Simplification of the technique seems to weaken the bond strength to tooth structure.

10. To create a hydrolytically stable bond to dentin the practitioner must:
    a. Use an acidic solvent.
    b. Apply a solvent free adhesive layer in a separate step.
    c. Use a hydrophilic monomer.
    d. Use only an ethanol solvent containing bonding agent.

11. When mechanically preparing a cavity preparation the process will:
    a. Not remove all of the bacterial laden dentin.
    b. Allow for the recurrence of caries if even minimal microleakage occurs.
    c. Require disinfection and eradication of the bacterial contamination.
    d. All of the above.

12. When our preparations for direct and indirect restorations end on cementum:
    a. We can treat the process as if we ended on enamel.
    b. Microleakage is less.
    c. Expectations would be for less micromechanical retention.
    d. We can bond to this area with more predictability.

13. The challenge of bonding to wet dentin can be addressed by the addition of:
    a. Hydrophilic primers.
    b. Acetone solvents in the bonding agent.
    c. Alcohol as a solvent.
    d. All of the above.

14. With increasing depth, our cavity preparations may demonstrate an increase in postoperative sensitivity because of:
    a. An increase in the number and size of dentinal tubules.
    b. An increase in the fluid flow from the dentinal tubules.
    c. A possibility that the materials may irritate the pulpal complex.
    d. All of the above.

15. When using a glutaraldehyde/HEMA combination:
    a. There is no adverse effect when using either acetone or alcohol as a solvent.
    b. One should use this combination only with an acetone solvent.
    c. One should use this combination only with an alcohol solvent.
    d. One should use a nonsolvent containing bonding agent.

16. The multiple benefits of using a glutaraldehyde/HEMA product after cavity preparation include:
    a. The eradication of all bacteria and have a post-application antibacterial effect.
    b. Stabilization and enhancing the bond to dentin because of its flocculating ability and cross-linking of the collagen with fourth- and fifth-generation bonding agents.
    c. Decrease postoperative sensitivity by blocking the dentinal tubules, and thereby eliminating fluid flow which is the primary cause of sensitivity.
    d. Do all the above including having no ill effects on cements used for crown and bridge.
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