The Immunomodulatory Properties of 2-Hydroxyethyl Methacrylate are Mediated by the NLRP3 Inflammasome.

J Adhes Dent. 2018 May 31;:1-8

Authors: Alizadehgharib S, Östberg AK, Larsson L, Dahlgren U

Abstract

PURPOSE: The methacrylate monomer 2-hydroxyethyl methacrylate (HEMA), commonly used in dentistry, has multiple effects on the immune system. This study examined whether HEMA affects the immune system by inducing formation of the NLRP3 inflammasome.

MATERIALS AND METHODS: Human peripheral blood mononuclear cells (PBMCs) and the human monocyte cell line THP1 were cultured with or without 1000 μM HEMA. To block NLRP3 inflammasome activation, 130 mM KCl was also added to some of the cultures. For the in vivo studies, two different experimental setups were used. In the first experimental setup, mice were injected subcutaneously at the base of the tail with 20 μmol HEMA with or without 100 mM KCl. After 3 weeks, the animals were given an identical booster injection. Two weeks after the last injection, the mice were sacrificed and splenectomized. In the second experimental setup, HEMA (20 μmol), with or without 100 mM KCl, was injected subcutaneously into the tails of BALB/c mice. The mice were given two similar injections at 3-week intervals to allow evaluation of the local inflammation induced by HEMA. After the last inoculation, the injection site was examined daily for 4 days, after which the mice were sacrificed.

RESULTS: Cultures of PBMCs and THP1 cells exposed to HEMA in vitro produced more IL-1β and IL-18 than did control cells. Increased extracellular concentration of KCl inhibited the secretion of IL-1β. HEMA exposure did not induce cytokine
production in variants of the THP1 cell line unable to form the NLRP3 inflammasome. For the first experimental setup, the level of unstimulated basic splenocyte proliferation in vitro was significantly higher in cultures from mice exposed in vivo to HEMA only than in cultures from mice injected with HEMA plus KCl. In the second experimental setup of the in vivo studies, the HEMA-treated mice developed more pronounced inflammation at the site of injection compared to the group of mice given HEMA plus KCl. CONCLUSION: HEMA affects the immune system by inducing formation of the NLRP3 inflammasome.

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20 wt%, 30 wt%, 40 wt%) were added to a model adhesive system consisting of TEG-DMA (25 wt%), UDMA (20 wt%), HEMA (30 wt%), water (4 wt%), camphorquinone (0.5 wt%), and tertiary amine (0.5 wt%) dissolved in 20% acetone (A12, A20, A30 and A40) or 20% ethanol (E12, E20, E30 and E40). DC% was evaluated by FT-IR spectroscopy. Human molars were wet ground until the occlusal dentin was exposed, the adhesive systems were applied after 37% phosphoric acid etching, and resin composite buildups were incrementally constructed. After storage in distilled water at 37°C for 24 h, the teeth were cut into resin-dentin beams (cross-sectional area 1 mm2). Microtensile bond strength (μTBS) was evaluated after 24 h, 6 months, and 1 year of water storage at 37°C. The failure mode was categorized as adhesive, mixed, or cohesive. Data were analyzed using ANOVA and Tukey’s HSD test (a = 0.05).

RESULTS: A12 presented the lowest DC% (p < 0.05). All the other adhesive systems showed statistically similar DC% (p > 0.05). All adhesive systems maintained resin-dentin bond stability after 6 months of water storage, while only A40 and E40 maintained it after 1 year.

CONCLUSION: Irrespective of the type of organic solvent, the incorporation of high concentrations of 4-META (40 wt%) improved the resin-dentin bond stability of the experimental etch-and-rinse adhesive systems over a period of 1 year.

(27869252)
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Effect of HEMA Phosphate as an Alternative to Phosphoric Acid for Dentin Treatment Prior to Hybridization with Etch-and-Rinse Adhesive Systems.

J Adhes Dent. 2016 Sep 23;

Authors: Foscaldo T, Dos Santos GB, Miragaya LM, Garcia M, Hass V, da Silva EM

Abstract

PURPOSE: To evaluate the effect of dentin treatment using HEMA phosphate (HEMA-P) on the microtensile bond strength (μTBS) and nanoleakage of an etch-and-rinse adhesive system.

MATERIALS AND METHODS: The occlusal surfaces of human molars were wet ground until superficial dentin was exposed. The specimens were then assigned to two groups according to dentin treatment: PA: 37% H₃PO₄ for 15 s; or HP: HEMA-P for 15 s. Adper Single Bond 2 was applied to the treated dentin surfaces and resin composite buildups were incrementally constructed over them. After 24-h storage in artificial saliva at 37°C, the bonded teeth were cut into resin-dentin sticks with a cross-sectional area of 1 mm², which were submitted to μTBS testing immediately or after 3 months of storage in artificial saliva at 37°C. Nanoleakage was assessed using SEM/EDS, and the interaction between dentin and H₃PO₄ or HEMA-P was evaluated by combining micro-Raman and FT-IR spectroscopy. The data were analyzed using two-way ANOVA and Tukey's HSD post-hoc test (α = 0.05).

RESULTS: HP presented significantly higher μTBS than PA at both times (p < 0.05). Both treatments maintained μTBS stability after 3 months of artificial saliva storage (p > 0.005). At both times, PA presented higher nanoleakage than HP (p < 0.05).

CONCLUSIONS: Both dentin treatments maintained μTBS stability after 3 months of artificial saliva storage. The use of HEMA-P was associated with less nanoleakage than was traditional phosphoric-acid etching.

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Bond Strength of Experimental Low-viscosity Resin Materials to Early Enamel Caries Lesions: Effect of Diluent/Solvent Addition.

J Adhes Dent. 2015 Mar 31;

Authors: Araújo TG, Sfalcin RA, Araújo GS, Alonso RC, Puppin-Rontani RM

Abstract

PURPOSE: To evaluate the effect of different concentrations of monomers and solvents/diluents on the microtensile bond strength (μTBS) bond strength of experimental low-viscosity resins (infiltrants) to enamel caries-like lesions (ECLL).

MATERIALS AND METHODS: Flat enamel blocks obtained from sound human third molars were submitted to ECLL formation and randomly distributed into 9 groups (n = 10): G1: TEG-DMA 100%; G2: TEG-DMA 80%, ethanol 20%; G3: TEG-DMA 80%, HEMA 20%; G4: TEG-DMA 75%, UDMA 25%; G5: TEG-DMA 60%, UDMA 20%, ethanol 20%; G6: TEG-DMA 60%, UDMA 20%, HEMA 20%; G7: TEG-DMA 75%, bis-EMA 25%; G8: TEG-DMA 60%, bis-EMA 20%, ethanol 20%; G9: TEG-DMA 60%, bis-EMA 20%, HEMA 20%. After etching with 37% phosphoric acid for 60 s, experimental infiltrants were actively applied and photocured for 60 s, then stored in 100% humidity (24 h, 37°C). Hourglass-shaped specimens were obtained and the μTBS test performed (MPa). The fracture patterns were assessed by SEM. Data were submitted to two way-ANOVA and Tukey’s tests (α = 0.05).

RESULTS: The highest μTBS value was observed for G4 (TEG-DMA/UDMA, 19.18 MPa) and the lowest for G5 (TEG-DMA/UDMA/ethanol, 9.00 MPa). A significant decrease in μTBS was observed for all groups containing ethanol (G2, G5, and
G8). The addition of HEMA did not affect μTBS values. Most groups showed a high frequency of mixed failure between infiltrant and enamel. CONCLUSION: The addition of bis-EMA or UDMA to TEG-DMA-based infiltrants did not improve bond strength to carious enamel. The ethanol addition negatively affected the bonding strength of infiltrants to enamel caries-like lesions, regardless of the resin matrix composition of the infiltrant.

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**Replacing HEMA with Alternative Dimethacrylates in Dental Adhesive Systems: Evaluation of Polymerization Kinetics and Physicochemical Properties.**

J Adhes Dent. 2014 Mar 28;

Authors: Münchow EA, Zanchi CH, Ogliari FA, Silva MG, Oliveira IR, Piva E

Abstract

Purpose: To evaluate the mechanical and physical properties of experimental HEMA-containing and HEMA-free resin adhesives. Materials and Methods: Experimental HEMA-free adhesives containing alternative dimethacrylates (bis-EMA 10 [B10], bis-EMA 30 [B30], PEG 400 [P400], PEG 1000 [P1000], PEG 400
UDMA [UP400]) were formulated and compared with a HEMA-containing adhesive (control). The adhesives were characterized by rheological analysis, polymerization kinetics (PK), water sorption (WS), and solubility (SL) tests. Flexural strength (FS) and flexural modulus (E) tests were performed under dry or wet conditions (distilled water or 70% ethanol solution). One-way and two-way ANOVA as well as Tukey’s test were used to evaluate differences between groups (p < 0.05). Results: The control group showed the lowest viscosity and was the only one with a degree of conversion lower than 50%. The control and the P1000 adhesive showed the statistically significantly highest WS (p < 0.05). The control and the UP400 adhesive showed the highest FS and E, and the dry-stored specimens showed more improved mechanical strength than did the wet-stored specimens (p < 0.05). Conclusion: The physicomechanical properties of some of the HEMA-free adhesives were substantially improved when compared with those of the control, indicating that they could be potential monomers for the development of HEMA-free adhesive systems.

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Collagen cross linking increases its biodegradation resistance in wet dentin bonding.

J Adhes Dent. 2012 Feb;14(1):11-8

Authors: Xu C, Wang Y

Abstract
PURPOSE: The biodegradation of exposed dentin collagen within the
adhesive/dentin (a/d) interface is one of the main reasons for composite restoration failures and seriously affects the durability of dental restorations. In the present study, the objective was to investigate whether the inclusion of the cross-linking reagent (glutaraldehyde, GA) in the adhesive would increase collagen biodegradation resistance within the a/d interface.

MATERIALS AND METHODS: The model adhesive consisted of ~60 % monomers (HEMA/bis-GMA, 45/55 wt/wt) and ~ 40 % ethanol as a solvent. 5% GA was added to the above formulation. After the dentin surfaces were etched for 15 s with 35% phosphoric acid, rinsed with water and blotted dry, adhesives both with and without GA were applied and polymerized by visible light for 20 s. These a/d specimens were immersed in the biodegradation solution (prepared by adding 160 mg collagenase in 1 liter of TESCA buffer solution) for up to 30 days after proceeding with the sectioning/fracture to expose the a/d interfaces. The specimens were analyzed using SEM and micro-Raman spectroscopy.

RESULTS: SEM results indicated that for the adhesive without GA, there were many voids and a loss of collagen fibrils in the a/d interface after being challenged by the biodegradation solution. The Raman spectra collected from the interface showed that the amide I of collagen at 1667 cm-1 obviously decreased, indicating a removal of collagen fibrils during the degradation process. For the adhesive containing GA, the collagen fibrils within the interface did not degrade at all, which was also confirmed by the Raman results.

CONCLUSION: The results corroborate the previous findings that by using the current adhesive system and wet bonding, the collagen fibrils in the a/d interface are largely unprotected and easily undergo biodegradation. Directly including cross-linking agents in the adhesive could protect collagen fibrils from degradation in situ within the a/d interface.

(21594232)
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Influence of 2-hydroxyethyl methacrylate concentration on polymer network of adhesive resin.

J Adhes Dent. 2011 Apr;13(2):125-9

Authors: Collares FM, Ogliari FA, Zanchi CH, Petzhold CL, Piva E, Samuel SM

Abstract

PURPOSE: To evaluate the effect of variations in 2-hydroxyethyl methacrylate (HEMA) concentrations in an experimental comonomer blend on degree of conversion, water sorption, solubility, and ultimate tensile strength of adhesive resin.

MATERIALS AND METHODS: The effect of HEMA content (0, 15, 30, and 50%wt - control, G15, G30, and G50 groups, respectively) was tested in an experimental comonomer blend of bis-GMA, bis-EMA, TEG-DMA, and HEMA. The degree of conversion, polymerization rate, ultimate tensile strength, water sorption, and solubility of the adhesive resin blends were determined.

RESULTS: At 40 s of light activation time, groups G30 and G50 showed a decrease of 30% and 61%, respectively, in degree of conversion compared to control. Water sorption and solubility differed for all groups, and was statistically higher in G50. For ultimate tensile strength, the control and G15 groups showed statistically higher values than the other groups (p < 0.05).

CONCLUSION: Higher HEMA content increases dental adhesive resin degradation.

(21594225)
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Biological evaluation of 2-hydroxyethylmethacrylate (HEMA) toxicity in human gingival fibroblasts with histochemical X-ray microanalysis.

Abstract

PURPOSE: To analyze the cytotoxic effects of 2-hydroxyethylmethacrylate (HEMA) in human gingival fibroblasts using quantitative x-ray microanalysis (EXPMA) and two classical methods (DNA and LDH release in culture medium).

MATERIALS AND METHODS: Different concentrations of HEMA (5, 10, 20, 30, and 40 mM) in DMEM medium were used and the effects on human gingival fibroblasts after 6, 12, and 24 h were determined. As controls, fibroblasts cultured with DMEM culture medium (negative control) and fibroblast incubated in 1% triton X (positive control) were used.

RESULTS: The results showed that correlation between the concentrations of HEMA and the amount of LDH and DNA released to the medium were statistically significant for all times analyzed. LDH and DNA released from cells incubated in the lowest concentrations of HEMA (5 and 10 mM) were not significantly different to negative controls. In contrast, cells incubated in the highest HEMA concentrations (20, 30, 40 mM) showed a significant increase of both LDH and DNA released to the culture medium at 6, 12, and 24 h. On the other hand, the ionic concentration of the different elements analyzed in this work revealed that the contents of P, S, Cl, and K were significantly higher in the controls than in samples incubated for 6 h in 5 mM or 10 mM HEMA (p < 0.01). K/ Na index (an
excellent marker of cell viability) showed a significant decrease, and therefore, viability was significantly reduced.

CONCLUSION: The results suggest that EXPMA is a sensitive method that is able to detect early cell damage even before the cell membrane is altered.

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bur-cut enamel and dentin was determined using a standardized protocol and the respective adhesive/dentin interface of these adhesives was characterized by transmission electron microscopy. Statistical analysis was performed with the Kruskal-Wallis nonparametric test.

RESULTS: Regarding bond strength, the control adhesives tended to perform superior to the one-step adhesives. However, a significant difference between the control adhesives and some one-step adhesives could not always be demonstrated, partly due to the statistical setup of this study. Interface analysis by electron microscopy showed wide variation among the one-step adhesives, depending on their composition and their acidity. 1-SEAs also exhibited two different kinds of droplets, depending on their hydrophilicity. Hydrophobic HEMA-free 1-SEAs such as G-Bond were prone to phase separation, while especially HEMA-containing hydrophilic 1-SEAs, such as Clearfil S3 Bond and Xeno III were predisposed to forming osmosis-induced droplets. Hybrid bond, Absolute, and iBond featured both phase separation as well as osmosis. Optibond All-in-one exhibited a clustering reaction of the filler particles upon solvent evaporation. All adhesives including the control adhesives showed signs of nanoleakage, indicating that all adhesives are to some extent permeable to water. A definitive conclusion with regard to quantitative assessment of nanoleakage was much hindered by inconsistencies in the silver deposition. The application procedure of some 1-SEAs sometimes proved as elaborate and time consuming as those of the two-step adhesive Clearfil SE Bond.

CONCLUSION: Considering bond strength and application procedure, 1-SEAs are not always a better alternative to multistep adhesives.

(19603581)
.- indexed for MEDLINE]
Volatile methacrylates in dental practices.

J Adhes Dent. 2009 Apr;11(2):101-7

Authors: Marquardt W, Seiss M, Hickel R, Reichl FX

Abstract

PURPOSE: In recent years, an increase of occupational respiratory diseases, such as asthma caused by methacrylates, has been observed in dental personnel. In this study, the exposure of dental personnel to various volatile methacrylates was investigated.

MATERIALS AND METHODS: The air levels of methacrylates were measured during filling treatment while bonding agents were used in 4 dental practices in Munich, Germany. Short-term air sampling (15 min) was performed using solid phase microextraction (SPME). The SPME fibers were coated with carbowax/divinyl benzene to enrich the analytes. For analysis, the analytes were thermically desorbed from the fiber and subsequently analyzed directly by gas chromatography/mass spectrometry.

RESULTS: The methacrylates methyl methacrylate (MMA), 2-hydroxyethyl methacrylate (HEMA), ethylene glycol dimethacrylate (EGDMA), and triethylene glycol dimethacrylate (TEG-DMA) were identified in the air of dental practices. The exposure levels of the four methacrylates varied during the filling treatments. The maximum concentrations found were 0.4 mg/m3 for MMA, 45 microg/m3 for HEMA, 13 microg/m3 for EGDMA, and 45 microg/m3 for TEG-DMA. The detection of TEG-DMA correlated with the application of bonding agents during performance of dental fillings.

CONCLUSION: Exposure levels of different methacrylates were observed at all investigated dental practices. The maximum levels of MMA measured in this study were at least 200 times lower than the toxicologically relevant maximum allowable concentrations defined in various countries. Nevertheless, the exposure levels of methacrylates should be kept as low as possible due to the allergenic potential of some methacrylates.