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Changes in urinary bisphenol A concentrations associated with placement of dental composite restorations in children and adolescents

Nancy N. Maserejian, ScD; Felicia L. Trachtenberg, PhD; Olivia Brown Wheaton, BS; Antonia M. Calafat, PhD; Gayatri Ranganathan, MS; Hae-Young Kim, DrPH; Russ Hauser, MD, ScD, MPH

ABSTRACT

Background. Bisphenol A-glycidyl methacrylate (bis-GMA)–based dental composite restorations may release bisphenol A (BPA). The authors assessed changes in urinary BPA concentrations over a 6-month follow-up period in children and adolescents who received bis-GMA–based restorations.

Methods. The authors collected data from 91 study participants aged 3 to 17 years who needed composite restorations. Participants provided urine samples and information on BPA-related exposures before and at approximately 1 day, 14 days, and 6 months after treatment. The authors used multivariable linear regression models to test associations between the number of surface restorations placed and the changes in urinary BPA concentrations.

Results. Participants had a mean (standard deviation [SD]) of 1.4 (1.0) for surfaces restored with composite at the first treatment visit and 2.3 (1.6) for surfaces restored during the entire study period. Mean (SD) change in urinary BPA concentrations between pretreatment and day 1 was 1.71 (9.94) nanograms per milliliter overall and 0.87 (5.98) after excluding 1 participant who had 8 surfaces restored at the visit. Overall, the authors observed an association between a greater number of composite surface restorations placed and higher urinary BPA concentrations in the 1-day sample (posterior-occlusal exponentiated coefficients [e^{β}] = 1.47; 95% confidence interval [CI], 1.18-1.83; $P < .001$), but the association was attenuated after the authors restricted the sample to the 88 participants who had up to 4 restorations ($e^{\beta} = 1.19$; 95% CI, 0.86-1.64), and they did not observe any association using 14-day ($e^{\beta} = 0.94$; 95% CI, 0.75-1.18) or 6-month ($e^{\beta} = 0.88$; 95% CI, 0.74-1.04) samples.

Conclusions. Placement of bis-GMA–based restorations in children and adolescents may produce transient increases in urinary BPA concentrations that are no longer detectable in urine samples taken approximately 14 days or 6 months after treatment. After placement of a few restorations, increases in urinary BPA concentrations may not be detectable, owing to a high level of variation in background BPA exposure.

Practical Implications. These results suggest that leaching of BPA from newly placed composite restorations ceases to be detectable in urine within 2 weeks after restoration placement. The potential human health impact of such short-term exposure remains uncertain.

Key Words. Dental restoration; dental care for children; composites; pediatric dentistry; polymers; bisphenol A.

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Bisphenol A (BPA) is a chemical used in the manufacturing of polycarbonate plastics and epoxy resins, which are used by nearly every industry, including dentistry. Concern about human BPA exposure exists because BPA is an endocrine-disrupting chemical and because the results of animal studies have shown that BPA has reproductive, developmental, and systemic toxic effects even at low doses (for example, less than 50 milligrams per kilogram per day).[1-3] A causal role for BPA in human health problems remains to be determined, and most studies to date have been cross-sectional.[4,5] However, evidence from prospective human studies suggests that prenatal or postnatal exposure to BPA is associated with

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reproductive health measures (for example, ovarian toxicity in women[6] and delayed puberty in boys[7]), immune function,[8,9] and neurodevelopment in children.[4]

The possibility of adverse effects related to BPA exposure in humans has driven research efforts to identify BPA exposure sources, improve BPA exposure characterization in humans, and produce BPA-free substitute products.[10,11] The predominant exposure route in the general population appears to be through foods and beverages manufactured and stored using BPA-containing materials.[12-17] However, such products account for only approximately 20% of the BPA produced worldwide each year,[11] and the results of human biomonitoring studies suggest that nondietary exposure sources also exist.[18,19]

In dentistry, BPA is used to synthesize matrix monomers, such as bisphenol A-glycidyl methacrylate (bis-GMA), that are used commonly in composite restorative and sealant materials.[20] The BPA structure has benefits of bulk, rigidity, and strength.[21] An unfavorable feature of such composite materials is incomplete polymerization, which results in shrinkage, marginal leakage, and degradation over time.[21,22] Investigators of numerous studies have shown that composite materials release various chemicals, including BPA, into the oral environment.[23-25] In the largest human biomonitoring study of this issue to date,[26] investigators followed 172 adults for a maximum of 30 hours after the participants had received composite restorations. The investigators reported increases in BPA and other related compounds in study participants' saliva within 1 hour after restoration placement and an increased concentration of BPA in study participants' urine 9 to 30 hours after placement.[26] However, the time window of chemical release from composite restorations may extend past this initial placement period, throughout the life of the restoration, as the composite degrades over time.[24] The results of in vitro studies have indicated that storage time, as well as mechanical stress such as chewing, and the intake of acidic foods or beverages are associated with the release of chemical components of composite.[24,27,28] The extent to which BPA continues to be released over the long term remains unexamined in human biomonitoring studies. Even if the dose of BPA is considered low (that is, lower than the no-observed-adverse-effect-level) as indicated by the results of in vitro studies,[22] the possible chronic exposure to BPA may have an impact on health outcomes, because low levels of endocrine-disrupting chemicals are sufficient to cause adverse effects in animal studies.[2,29]

The possibility of adverse health effects related to composite restorations was reported by the investigators of the New England Children's Amalgam Trial (NECAT),[30] a 5-year clinical trial designed to test the safety of dental amalgam for restorations. Children who were randomly assigned treatment with composite restorations had worse psychosocial health outcomes after 4 to 5 years compared with children who were randomly assigned treatment with amalgam.[30] Further analysis showed that a greater level of treatment with composite restorations containing bis-GMA was associated with increased behavioral problems, certain neuropsychological measures, and, possibly, certain immune function markers.[31-33] However, randomization to composite restoration was not associated with study participants' physical development,[34] and there was no association between preventive sealants or other flowable composite materials and psychosocial or neuropsychological health.[35] In other trials, investigators have found that the dental materials tested released BPA, bisGMA, and related materials,[36-39] but the NECAT investigators did not measure the changes in children's urinary concentrations of BPA or other compounds that may leach from composite. Thus, the extent to which having composite restorations can lead to BPA exposure in children remains uncertain.

The aim of this study was to examine changes in urinary BPA concentrations in children and adolescents before and after placement of dental composite restorations up to 6 months after treatment.

METHODS

We designed the Composites and Urinary Bisphenol-A Study (CUBS) to examine changes in urinary BPA concentration in pediatric dental patients after placement of dental composite restorations throughout a follow-up period of approximately 6 months. The figure and Table 1 outline the enrollment eligibility criteria and provides details about the data collection visits. Study participants were recruited from 8 participating clinical sites in the greater Boston area: 2 academic hospital settings (School of Dental Medicine at Tufts University and Franciscan Hospital for Children), 3 community health centers (Cambridge Health Alliance, Lynn Community Health Center, and Edward M. Kennedy Community Health Center), 2 private practices, and 1 oral health research institute (The Forsyth Institute). A central institutional review board (IRB) and each participating clinical site's institutional IRB, including the IRB of the independent research organization, New England Research Institutes, approved the study. The analysis of masked specimens by the Centers for Disease Control and Prevention (CDC) laboratory was determined not to constitute engagement in human subjects research. We obtained written informed consent from the parent or

ABBREVIATION KEY. bis-GMA: Bisphenol A-glycidyl methacrylate. **BPA:** Bisphenol A. **CDC:** Centers for Disease Control and Prevention. **CUBS:** Composites and Urinary Bisphenol-A Study. **IRB:** Institutional review board. **NECAT:** New England Children's Amalgam Trial. **NHANES:** National Health and Nutrition Examination Survey. **NIEHS:** National Institute of Environmental Health Sciences.