A Prospective Cohort Study of Bisphenol A Exposure from Dental Treatment

Journal of Dental Research
2020, Vol. 99(11) 1262–1269
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for Dental Research 2020
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DOI: 10.1177/0022034520934725
journals.sagepub.com/home/jdr

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Abstract

Laboratory studies show that bisphenol A (BPA) leaches from bisphenol A-glycidyl methacrylate (bisGMA)-based dental materials. We aimed to quantify the extent to which children are exposed to BPA from dental treatment with bisGMA materials, by amount of treatment and type of sedation. We hypothesized that posttreatment urinary BPA (uBPA) concentrations would be higher among patients with more surfaces treated with bisGMA-based materials and among patients receiving general anesthesia compared with pretreatment concentrations. We conducted a prospective cohort study in 211 children, 4 to 12 y old, who had no prior resin-based dental treatment. We measured uBPA concentrations twice before treatment and at 2 d and 1, 4, and 16 wk posttreatment. We abstracted treatment data (surfaces treated) from the chart. We generated descriptive statistics and compared pre- and posttreatment uBPA concentrations using generalized estimating equations. Participants were 51% female, 46% non-White, and 74% publicly insured. The median age was 6 y. The mean number of tooth surfaces exposed to BisGMA materials (composites/sealants) was 7.5 (SD 5.3). Overall, uBPA concentrations were 86% higher (95% confidence interval [CI] 42% to 143%, $P < 0.001$) at 2 d posttreatment compared with pretreatment concentrations. The uBPA concentrations 2 d posttreatment versus pretreatment tended to be higher (112%, 95% CI 53% to 194%) among those receiving treatment on >4 surfaces than those receiving treatment on ≤ 4 surfaces (50%, 95% CI -2% to 130%). Two days after treatment, uBPA was significantly higher than pretreatment concentrations in children receiving nitrous oxide but not in those receiving general anesthesia. Among all findings, uBPA concentrations returned to baseline by 4 wk. Children experience short-term increases in BPA from dental treatment. The impact of relatively high, short-term BPA exposure on child health is unknown. Given the widespread use of BisGMA-based dental materials and that chronic low-dose BPA exposure may adversely affect child health, strategies that minimize BPA exposure could potentially improve child health.

Keywords: pediatric dentistry, composite materials, resins, sealants, epidemiology, dental materials

Introduction

In laboratory studies, bisphenol A (BPA) leaches from a wide range of bisphenol A-glycidyl methacrylate (bisGMA)-based dental materials at detectable levels (Olea et al. 1996; American Dental Association 2014a, 2014b). Most clinical studies in humans that have examined BPA exposure from dental treatment are small, short-term, or in adults (Joskow et al. 2006; Kingman et al. 2012; Berge et al. 2019). The degree to which BPA concentrations are elevated or sustained is not well characterized. A single prospective cohort study in 88 children found that urinary BPA (uBPA) concentrations increased at 1 d after treatment with bisGMA-based composite restorations and returned to baseline at 2 wk (Maserejian et al. 2016). However, this study examined relatively modest amounts of treatment and did not examine BPA exposure from dental sealants or dental-related BPA exposure from other sources. Individuals may be exposed to BPA during dental treatment from materials used in sedation such as FDA-approved products like nasogastric tubes and intravenous administration sets (Advanced Medical Technology Association 2008). BPA exposure may

also be modulated by barriers such as a rubber dam (Kingman et al. 2012).

BPA is an endocrine-disrupting chemical that has adverse effects at critical developmental time points (e.g., in utero, puberty) (Diamanti-Kandarakis et al. 2009; Yu et al. 2011; Berger et al. 2018). General population-level exposure to BPA can alter estrogen receptor-mediated actions involving transcription and cell membrane pathways that affect brain and reproductive development (vom Saal and Hughes 2005; Richter et al. 2007; Yolton et al. 2011). Available evidence

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A supplemental appendix to this article is available online.

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suggests child BPA exposure is positively associated with adverse health including obesity (Trasande et al. 2012), asthma (Donohue et al. 2013; Buckley et al. 2018), and adverse cognition and behavior (Braun et al. 2011); however, there are inconsistencies in findings (Maserejian et al. 2012; Braun 2017). Although food-related sources are believed to account for the majority of BPA exposure (74%), it has been suggested that dental sealants could account for as much as 17% of BPA exposure in children (von Goetz et al. 2010).

We set out to better understand the extent and duration of dental-related BPA exposure by types of dental materials and sedation. Our primary objective was to quantify the change in magnitude of overall dental-related BPA exposure in a large cohort of children to determine whether BPA exposure is sustained beyond the immediate posttreatment period. We hypothesized that posttreatment uBPA concentrations would be significantly higher than pretreatment concentrations among children exposed to more bisGMA-based dental materials and children receiving general anesthesia. Last, we explored the impact of using barriers (e.g., rubber dam) on uBPA concentrations.

Methods

Study Design

We conducted a prospective cohort study enrolling 211 children aged 4 to 12 y from the Center for Pediatric Dentistry at the University of Washington. Eligible participants had no prior resin-based dental exposure based on dental examination by a clinic dentist, had a treatment plan requiring bisGMA-based materials, met the American Society of Anesthesiologists classification I/II indicating the child was in good health, and lived within 30 miles of the clinic. We excluded children with physician-diagnosed developmental delay and those unable to provide urine. Eligible children who required bisGMA-based treatment with dental sealants and/or restorative treatment were identified at an assessment visit. Data collection occurred between January 2016 and September 2018. Because BPA exposure may vary based on amount of treatment and type of sedation, we aimed to recruit equal numbers of children receiving high and low amounts of anticipated treatment with bisGMA-containing materials (≤ 4 and >4 surfaces, determined at the assessment visit) and receiving different types of sedation (no sedation, nitrous oxide, and general anesthesia). Due to small numbers, children requiring oral sedation were not recruited.

Measurement

We assessed uBPA concentrations twice before treatment: once at the assessment visit and again at the treatment visit immediately prior to treatment. We measured posttreatment uBPA at 2 d and 1, 4, and 16 wk after treatment. Study visits took place in clinic or at the child's home. At each visit, a urine sample was collected using BPA-free containers, with time of collection

documented. We measured specific gravity on each sample to account for urinary dilution. Samples were aliquoted into BPA-free cryovials using a disposable BPA-free pipette, stored at -80°C , and analyzed in 3 batches.

At baseline and each follow-up survey, we asked about past 24-h BPA exposure to canned foods because this is a known source of high BPA exposure. Baseline exposure to canned foods was based on having reported consumption at either of the two pretreatment visits. We measured height and weight and collected demographic and health data at baseline. We abstracted treatment data from the chart identifying tooth, surface and type of materials placed, type of sedation, and type of isolation. The same resin-based dental composite (3M Filtek Supreme Ultra) and dental sealant (Ultrasal XT Plus by Ultradent) were used throughout the study. For children with multiple visits, we abstracted dental treatment data from each visit and conducted the 2-d follow-up visit and subsequent time points starting with the last treatment visit.

BPA Analysis

We determined free and total uBPA using an approach that involved the enzymatic deconjugation of BPA from its glucuronidated form, direct injection, and separation using high-performance liquid chromatography interfaced with a triple quadrupole mass spectrometer (Volkel et al. 2005; Volkel et al. 2008; Markham et al. 2010). The internal standard analytical method entailed a 9-point calibration ($R^2 > 0.999$) with quality control measures to monitor accuracy by spike recovery (SR) samples run at a 1:20 (5%) frequency (mean SR efficiency per batch ranged from 96% to 101%), blanks, and deconjugation efficiency determination by surrogate addition ($>85\%$ criteria met on all but 2 samples). Samples not within criteria were flagged, with all batches demonstrating efficient deconjugation (averages $>98\%$). Continuing calibration verification samples were injected at a 5% frequency with relative percent error (RPE) criteria ($\pm 10\%$) met on all batches. Replicate injections were performed at a 1:10 (10%) frequency, with relative percent difference (RPD) criteria ($\pm 25\%$) met on all samples above the 0.3 ng/mL reporting limit. Mean RPD was similar between batches: 9.2%, 7.9%, and 9.9%, respectively.

Data Analysis

We estimated proportions, means, standard deviations (SD), medians, and interquartile ranges (IQR) to describe demographics, sources of BPA, and dental treatment characteristics. For the primary analysis, we compared a continuous specific-gravity adjusted uBPA estimate at each posttreatment visit to the average of the two pretreatment uBPA measures. For uBPA measurements below the limit of detection (LOD), we imputed values with the LOD/2 method (Fu et al. 2016). Comparisons were based on geometric means in ng/mL because the distribution was skewed. We reported results as ratios (e.g., a ratio of 1.50 corresponds to a 50% increase). Analyses were conducted by fitting linear regression models to the logarithm of the ratio

of uBPA to specific gravity, using generalized estimating equations with the family as the clustering unit and an independent working correlation structure. Confidence intervals and *P* values were obtained using robust standard errors, and hypothesis tests were conducted using robust Wald tests. The model included fixed effects for posttreatment visit number (3, 4, 5, 6). We powered the study to detect a 25% increase in overall uBPA concentrations from pre- to posttreatment with 80% power and alpha of 0.05 with 210 children.

We conducted stratified analyses by (i) number of treatment visits (1 or 2 to 4); (ii) number of surfaces treated with bisGMA-based composites or sealant (>4 or ≤ 4); (iii) number of surfaces treated with composite restorations (>2 or ≤ 2); (iv) number of surfaces treated with sealants (>2 or ≤ 2); and (v) type of sedation at last treatment visit (general anesthesia, nitrous oxide, no sedation). We examined uBPA concentrations by type of isolation at last treatment visit. Tests of interaction between treatment and each stratification variable were conducted using robust Wald tests. We examined the time course of uBPA over time since treatment by plotting geometric means as a function of days since treatment and fitting an inverse-polynomial model of order 2 to log-transformed values.

To assess our assumptions, we conducted sensitivity analyses (i) on demographics, body mass index, and past 24-h canned foods, (ii) without adjustment for specific gravity, (iii) using multiple imputation of nondetects, (iv) excluding outliers, (v) adjusting for batch, (vi) comparing posttreatment with only the second pretreatment uBPA concentration, and (vi) on primary and permanent molars and incisors/canines. All analyses were conducted using R software. Subjects' rights were protected by the University of Washington institutional review board (#STUDY00001517). We obtained written informed consent from parents, verbal assent from children age 4 to 6, and signed assent from children age 7 to 12 y. This work conforms to the STROBE guidelines.

Results

At baseline, participants were on average 6 y old, 51% female, and ethnically/racially diverse (Table 1). Recent exposure to other sources of BPA was low (10% consumed canned food 24 h prior to dental treatment). Among the 211 children enrolled, 194 received dental treatment and are therefore included in the analysis. The remaining 17 patients did not return for their treatment visit ($n = 8$) or did not complete treatment for various reasons (e.g., refusal, child uncooperativeness). We collected 1,105 (95%) urine samples from 1,164 possible study visits.

Among the 194 participants receiving treatment, an average of 7.5 surfaces per child were treated with bisGMA-based materials, including 3.9 surface restorations and 3.6 surface sealants (Table 2). Most participants (73%) had all treatment at a single visit. At the only or last treatment visit, 28% participants received general anesthesia, 36% received nitrous oxide, and 36% received no sedation. A rubber dam was used for 57% of the participants. Of the 111 patients with a rubber dam, 105 had a rubber dam at all treatment visits.

There was a statistically significant 86% increase in uBPA concentrations between pretreatment and 2-d posttreatment (95% confidence interval [CI] 42% to 143%, $P < 0.001$, Table 3). Equivalently, the ratio of geometric mean specific-gravity adjusted uBPA was 1.86 (95% CI 1.42 to 2.43). In absolute terms, the geometric mean of uBPA increased from 0.51 ng/mL and 0.57 ng/mL at the two pretreatment visits, respectively, to 1.00 ng/mL at the 2-d posttreatment visit. The uBPA concentrations remained slightly elevated at 1-wk post treatment (28%, 95% CI 0% to 64%), and returned to pretreatment levels by 4 wk (2%, 95% CI -22% to 32%).

Participants with more than 4 surfaces treated with bisGMA-based materials (or bisGMA-based composites) had qualitatively higher uBPA concentrations than those who had 4 or fewer surfaces treated at 2 d posttreatment (Table 3); uBPA concentrations subsequently returned to baseline for both groups by 4 wk. Similarly, increases in uBPA posttreatment were qualitatively slightly higher for participants who had 2 to 4 treatment visits (as measured 2 d after their last visit) than those with a single treatment visit at 2 d posttreatment, with uBPA concentrations subsequently returning to baseline by 4 wk. Interactions between pretreatment and 2-d posttreatment by amount of treatment ($P = 0.07$) or number of treatment visits ($P = 0.72$) were not statistically significant. Increases in uBPA concentrations by type of sedation were highest among participants receiving nitrous oxide at 2 d posttreatment. Interactions by type of sedation were not statistically significant. Geometric mean uBPA concentrations declined quickly after treatment (Fig.). The decline in uBPA as a function of days since treatment was statistically significant ($P < 0.001$).

Estimated increases in uBPA at the 2-d posttreatment time point were overall similar for most subgroups including age, body mass index, parent education, insurance type, low pretreatment uBPA, and prior 24-h canned food consumption (Appendix Table 1). Boys had the largest increase in uBPA (125%, 95% CI 57% to 223%, $P < 0.001$), but girls also had a statistically significant increase in uBPA at the 2-d posttreatment time point (53%, 95% CI 5% to 123%, $P = 0.03$). The interaction by sex was not statistically significant ($P = 0.50$).

Results for sensitivity analyses were similar to the primary analysis (Appendix, Table 2). The uBPA unadjusted for specific gravity had no impact on our findings. Because 557 of the 1,105 (50%) of samples were below the limit of detection (Table 3), we evaluated multiple imputation of nondetects, which also showed no material differences compared with our overall results. Excluding outliers had little impact on our results, as did adjustment for batch, comparing posttreatment uBPA concentrations to the single pretreatment uBPA concentrations collected at the treatment visit. No differences in uBPA were observed for findings in permanent or primary molars and incisors/canines (data not shown). Details on treatment windows, location, number of days after treatment, and time of study visits are in the Appendix (Appendix Tables 3 and 4, Appendix Figs. 1 and 2).

Discussion

We found that posttreatment uBPA concentrations compared with pretreatment were 86% higher 2 d after treatment. The uBPA concentrations returned to baseline 4 wk after treatment. This trajectory was similar across subgroups.

Our findings related to the trajectory of dental-related BPA exposure are consistent with the other cohort study in children, which found that bisGMA-based materials increased in the short-term and returned to baseline by 2 wk posttreatment (Maserejian et al. 2016). The relative increase in the period immediately after treatment in our study is higher than that reported by Maserejian et al. (86% vs. 51%) and higher than that reported in adults (43%) (Kingman et al. 2012). The difference in magnitude may be because children in our study had more surfaces treated with bisGMA materials (mean = 7.5) than the other studies, which had, on average, fewer than 2.5 surfaces treated with resin-based materials. This is supported by our finding that qualitatively, those receiving more composites had higher uBPA concentrations than those receiving less treatment. In absolute terms, uBPA concentrations in our study were lower than those reported other US studies (Kingman et al. 2012; Maserejian et al. 2016; Lehmler et al. 2018). Evidence suggests that BPA concentrations in the United States have declined over time, and our geometric means are similar to lower, recent estimates (Ye et al. 2015).

Maserejian et al. (2016) enrolled a wider age range of ages (3 to 17 y), studied bisGMA-based composites but not sealants, used different composite material, and included individuals with prior composite exposure. Despite these differences, our results are consistent with those of Maserejian et al. Thus, our findings strengthen and clarify the body of evidence regarding the trajectory of BPA exposure from dental treatment. BPA leaches from multiple brands of bisGMA-based composites, suggesting this is not a brand-dependent effect.

That the increase in dental treatment-related BPA exposure was short-term suggests that residual BPA does not continue to be leached. Our finding is consistent with the assertion that exposure is from short-term leaching of residual unpolymerized material on the surface of the sealant or restoration that remains after the curing process (American Dental Association 2014b; Maserejian et al. 2016). Leaching from degradation of bisGMA-based dental materials over longer periods of time remains an open question.

FDA-approved medical products used in dental anesthesia contain BPA (Advanced Medical Technology Association 2008). We hypothesized that children receiving treatment under general anesthesia would have higher exposure to BPA. We did not observe this. Instead, children receiving treatment with nitrous oxide had the highest increase in uBPA concentrations immediately after treatment. Children receiving nitrous oxide are continuously, orally exposed to plastic tubing throughout the procedure, which may explain this finding. Other possibilities are that the vapor itself contains BPA or that this finding occurred by chance.

BisGMA-based composites and sealants are the most commonly used materials in dentistry (American Dental Association

Table 1. Characteristics of Study Participants (N = 194).

Age, y, median (IQR)	6 (5 to 7)
Age categories, n (%)	
4 to 5 y	76 (39)
6 to 7 y	71 (37)
8 to 9 y	34 (18)
10 to 12 y	13 (7)
Female, n (%)	98 (51)
Child body mass index percentile category, n (%)	
<85th percentile	147 (76)
≥85th to 95th percentile	19 (10)
≥95th percentile	28 (14)
Race, n (%) [N = 178]	
American Indian/Alaska Native	3 (2)
Asian	20 (11)
Black or African American	23 (13)
White	96 (54)
More than one race	36 (20)
Hispanic, n (%) [N = 173]	35 (20)
Primary language spoken at home, n (%)	
English	150 (77)
Spanish	14 (7)
Other	30 (15)
Family income, n (%) [N = 177]	
0 to \$30,000	57 (32)
\$30,000 to \$60,000	52 (29)
\$60,000 to \$150,000	42 (24)
>\$150,000	26 (15)
Primary parent's education, n (%)	
Less than high school or high school graduate	39 (20)
Some college or trade/technical/vocational training	61 (31)
College graduate	46 (24)
Some postgraduate work or postgraduate degree	48 (25)
Child's insurance, ^a n (%)	
Private	50 (26)
Public or no insurance	144 (74)
Marital status, n (%)	
Married	117 (60)
Separated, divorced, or widowed	27 (14)
Never married	50 (26)
Consumed canned food in 24 h prior to treatment visit, n (%)	19 (10)

^aPublic includes Medicaid, Apple Health, and Molina. Participants with both public and private insurance were classified as Private.

2007). Nearly 30 million children have a dental restoration, and over 28 million children have dental sealants (Griffin et al. 2016; Fleming and Dafful 2018; National KIDS COUNT 2019). More than 85% of composites use BPA derivatives. BisGMA is an ingredient in nearly two-thirds of sealants, whereas 15% of dental composites do not use BPA (Dursun et al. 2016; Fleisch et al. 2010). The World Dental Federation discourages the use of BPA in the manufacture of dental materials (FDI World Dental Federation 2013). Nevertheless, the use of bisGMA in dental materials is widespread because it has essential physical properties (stiffness, hardness) that ensure longevity (American Dental Association 2014a). Its widespread use means that at a population level, dental treatment is a common source of BPA exposure. The impact of dental-related BPA exposure on individual-level health, however, is

Table 2. Dental Treatment Characteristics for Study Participants (N = 194).

Number of surfaces treated, mean $\pm$ SD, median (IQR)	
Total, with any type of material	17.0 $\pm$ 16.4, 9 (5 to 25.5)
BisGMA-based composite and sealants	7.5 $\pm$ 5.3, 6 (4 to 10.8)
BisGMA-based composite	3.9 $\pm$ 5.2, 2.5 (0 to 6)
BisGMA-based sealants	3.6 $\pm$ 3.5, 4 (0 to 5.8)
Amalgam	0.0 $\pm$ 0.0, 0 (0 to 0)
Glass ionomer	1.6 $\pm$ 4.2, 0 (0 to 0)
Stainless steel	7.5 $\pm$ 12.2, 0 (0 to 10)
Other ^a	0.4 $\pm$ 2.4, 0 (0 to 0)
Number of teeth extracted, mean $\pm$ SD, median (IQR)	0.5 $\pm$ 1.2, 0 (0 to 0)
Type of sedation, n (%)	
General anesthesia	55 (28)
Nitrous oxide	69 (36)
None	70 (36)
Type of barrier, n (%)	
Rubber dam	111 (57)
Isolite	68 (35)
Cotton rolls/none	15 (8)
Number of treatment visits, n (%)	
1	141 (73)
2	32 (16)
3	12 (6)
4	9 (5)
Days between last pretreatment uBPA and first posttreatment uBPA among those with >1 treatment visit, mean $\pm$ SD, median (IQR)	41.1 $\pm$ 36.9, 30 (19 to 52)
Number of surfaces restored with BisGMA-based composite, mean $\pm$ SD, median (IQR)	
1 treatment visit	3.2 $\pm$ 5.5, 1 (0 to 4)
2 to 4 treatment visits	5.8 $\pm$ 3.8, 5 (4 to 8)
Number of surfaces treated with BisGMA-based sealants, mean $\pm$ SD, median (IQR)	
1 treatment visit	3.4 $\pm$ 3.4, 3 (0 to 6)
2 to 4 treatment visits	3.9 $\pm$ 3.5, 4 (0 to 5)
Number of surfaces treated with BisGMA-based composite or sealants, mean $\pm$ SD, median (IQR)	
1 treatment visit	6.6 $\pm$ 5.5, 5 (4 to 8)
2 to 4 treatment visits	9.8 $\pm$ 4.2, 9 (6 to 12)

BisGMA, bisphenol A-glycidyl methacrylate; IQR, interquartile range; uBPA, urinary bisphenol A.

^a“Other” includes zirconia, silver diamine fluoride, and surface smoothing with finishing bur.

unclear. Unlike food and beverages (common sources of BPA), dental treatment is not a continuous exposure and the body of evidence now suggests that when dental treatment occurs, exposure is time-limited.

Although the extent to which relatively high short-term increases in BPA exposure affect child health is unknown, given that BPA exposure likely affects child health and considering the World Dental Federation’s recommendations, minimizing dental-related BPA exposure would be prudent (FDI World Dental Federation 2013). Ambient exposure to BPA has been associated with adverse health effects in children (Braun et al. 2011; Trasande et al. 2012; Donohue et al. 2013; Trasande et al. 2013; Buckley et al. 2018). Thus, cumulative exposure to BPA is a health concern, and dental-related BPA is a specific, identifiable, short-term source of exposure. Our findings did not corroborate the findings of others (Kingman et al. 2012) who reported that rubber dams protect against BPA exposure. Approaches to minimize BPA exposure during dental treatment such as additional gargling, greater suction, more air/spray washing, or using other materials (e.g., glass ionomer) should be evaluated. Given that BPA exposure increases after

each treatment visit (Maserejian et al. 2016), reducing the number of treatment visits when feasible may also reduce BPA exposure.

One unique strength of this study is that we did not ask participants to change their behavior to decrease BPA exposure before dental treatment. The other cohort studies asked participants to refrain from eating canned foods to ensure that any effects detected would not be attributable to exposures other than dental treatment (Kingman et al. 2012; Maserejian et al. 2016). Thus, this study adds to the body of knowledge by showing the trajectory of BPA exposure from dental treatment in the course of everyday life.

Half of the samples did not have detectable uBPA concentrations. Population data suggest that uBPA concentrations are declining (Calafat et al. 2008; Ye et al. 2015). Reduction in BPA in canned foods may explain this occurrence (Green Century Capital 2010). Our sensitivity analysis using multiple imputation methods for values below the limit of detection showed a similar finding to our overall result. Other sensitivity analyses that excluded outliers and used the pretreatment uBPA value on the day of treatment as the comparator did not alter

Table 3. Comparison of Specific-Gravity Adjusted uBPA Concentrations (ng/mL) for Collected Urine Samples by Study Visit.

	Pretreatment (N = 186)	Treatment (N = 185)	2-d Posttreatment (1 to 4 d ^a) (N = 183)	1-wk Posttreatment (5 to 20 d ^a) (N = 186)	4-wk Posttreatment (21 to 35 d ^a) (N = 183)	16-wk Posttreatment (4 to 24 wk ^a) (N = 182)
Overall						
Geometric mean uBPA	0.51	0.57	1.00	0.69	0.55	0.57
95% CI	(0.41 to 0.63)	(0.46 to 0.71)	(0.77 to 1.32)	(0.55 to 0.87)	(0.44 to 0.69)	(0.46 to 0.69)
Ratio	Reference	Reference	1.86	1.28	1.02	1.05
95% CI			(1.42 to 2.43)	(1.00 to 1.64)	(0.78 to 1.32)	(0.82 to 1.35)
Number of surfaces treated with BisGMA-based composite and sealants combined						
>4 surfaces (n = 119)						
Geometric mean uBPA	0.48	0.67	1.20	0.65	0.58	0.55
95% CI	(0.37 to 0.63)	(0.52 to 0.86)	(0.86 to 1.68)	(0.50 to 0.86)	(0.43 to 0.77)	(0.43 to 0.71)
Ratio	Reference	Reference	2.12	1.15	1.02	0.97
95% CI			(1.53 to 2.94)	(0.87 to 1.53)	(0.74 to 1.40)	(0.70 to 1.36)
≤4 surfaces (n = 74)						
Geometric mean uBPA	0.56	0.45	0.75	0.76	0.51	0.59
95% CI	(0.41 to 0.76)	(0.31 to 0.63)	(0.49 to 1.14)	(0.50 to 1.15)	(0.35 to 0.72)	(0.42 to 0.82)
Ratio	Reference	Reference	1.50	1.52	1.02	1.18
95% CI			(0.98 to 2.30)	(0.97 to 2.38)	(0.66 to 1.55)	(0.82 to 1.70)
Number of surfaces restored with BisGMA-based composites						
>2 surfaces (n = 96)						
Geometric mean uBPA	0.51	0.62	1.21	0.70	0.61	0.50
95% CI	(0.38 to 0.69)	(0.47 to 0.83)	(0.84 to 1.74)	(0.51 to 0.97)	(0.44 to 0.85)	(0.37 to 0.66)
Ratio	Reference	Reference	2.14	1.24	1.08	0.88
95% CI			(1.51 to 3.02)	(0.92 to 1.67)	(0.76 to 1.55)	(0.61 to 1.26)
≤2 surfaces (n = 97)						
Geometric mean uBPA	0.51	0.53	0.83	0.68	0.49	0.64
95% CI	(0.39 to 0.67)	(0.39 to 0.72)	(0.56 to 1.23)	(0.48 to 0.96)	(0.36 to 0.68)	(0.48 to 0.86)
Ratio	Reference	Reference	1.60	1.32	0.96	1.24
95% CI			(1.08 to 2.39)	(0.89 to 1.96)	(0.67 to 1.37)	(0.87 to 1.76)
Number of surfaces treated with BisGMA-based sealants						
>2 surfaces (n = 106)						
Geometric mean uBPA	0.46	0.55	0.95	0.62	0.49	0.56
95% CI	(0.35 to 0.60)	(0.42 to 0.72)	(0.66 to 1.37)	(0.46 to 0.84)	(0.37 to 0.65)	(0.44 to 0.72)
Ratio	Reference	Reference	1.90	1.23	0.98	1.11
95% CI			(1.30 to 2.77)	(0.87 to 1.75)	(0.70 to 1.36)	(0.79 to 1.57)
≤2 surfaces (n = 87)						
Geometric mean uBPA	0.58	0.60	1.07	0.79	0.63	0.58
95% CI	(0.43 to 0.79)	(0.43 to 0.85)	(0.73 to 1.56)	(0.55 to 1.14)	(0.45 to 0.90)	(0.41 to 0.81)
Ratio	Reference	Reference	1.80	1.34	1.07	0.97
95% CI			(1.26 to 2.58)	(0.94 to 1.89)	(0.72 to 1.60)	(0.67 to 1.40)
Number of treatment visits						
1 visit (n = 140)						
Geometric mean uBPA	0.56	0.61	0.99	0.66	0.59	0.53
95% CI	(0.44 to 0.70)	(0.47 to 0.78)	(0.74 to 1.35)	(0.50 to 0.86)	(0.45 to 0.77)	(0.42 to 0.68)
Ratio	Reference	Reference	1.71	1.13	1.01	0.92
95% CI			(1.27 to 2.32)	(0.84 to 1.53)	(0.75 to 1.36)	(0.68 to 1.23)
2 to 4 visits (n = 53)						
Geometric mean uBPA	0.41	0.49	1.03	0.79	0.47	0.66
95% CI	(0.27 to 0.61)	(0.34 to 0.73)	(0.58 to 1.84)	(0.50 to 1.24)	(0.29 to 0.73)	(0.47 to 0.93)
Ratio	Reference	Reference	2.29	1.76	1.03	1.47
95% CI			(1.32 to 3.99)	(1.17 to 2.64)	(0.61 to 1.75)	(0.94 to 2.31)
Type of sedation						
General anesthesia (n = 55)						
Geometric mean uBPA	0.68	1.22	1.33	0.73	0.96	0.48
95% CI	(0.45 to 1.03)	(0.84 to 1.77)	(0.85 to 2.06)	(0.50 to 1.07)	(0.62 to 1.49)	(0.32 to 0.71)
Ratio	Reference	Reference	1.47	0.82	1.06	0.53
95% CI			(0.96 to 2.27)	(0.57 to 1.16)	(0.68 to 1.67)	(0.35 to 0.80)
Nitrous oxide only (n = 69)						
Geometric mean uBPA	0.46	0.47	1.02	0.67	0.51	0.58
95% CI	(0.32 to 0.66)	(0.34 to 0.65)	(0.64 to 1.62)	(0.45 to 1.00)	(0.36 to 0.72)	(0.42 to 0.80)
Ratio	Reference	Reference	2.18	1.44	1.09	1.24
95% CI			(1.39 to 3.42)	(0.95 to 2.16)	(0.70 to 1.70)	(0.83 to 1.85)

(continued)

Table 3. (continued)

	Pretreatment (N = 186)	Treatment (N = 185)	2-d Posttreatment (1 to 4 d ^a) (N = 183)	1-wk Posttreatment (5 to 20 d ^a) (N = 186)	4-wk Posttreatment (21 to 35 d ^a) (N = 183)	16-wk Posttreatment (4 to 24 wk ^a) (N = 182)
No sedation (n = 69)						
Geometric mean uBPA	0.46	0.42	0.81	0.70	0.39	0.65
95% CI	(0.34 to 0.62)	(0.30 to 0.60)	(0.51 to 1.31)	(0.45 to 1.08)	(0.27 to 0.55)	(0.47 to 0.90)
Ratio	Reference	Reference	1.85	1.59	0.88	1.48
95% CI			(1.14 to 3.01)	(0.98 to 2.56)	(0.59 to 1.32)	(0.95 to 2.29)
Type of barrier						
Rubber dam (n = 110)						
Geometric mean uBPA	0.53	0.71	1.20	0.74	0.69	0.52
95% CI	(0.40 to 0.70)	(0.54 to 0.94)	(0.85 to 1.69)	(0.55 to 1.00)	(0.51 to 0.93)	(0.40 to 0.68)
Ratio	Reference	Reference	1.96	1.21	1.13	0.84
95% CI			(1.42 to 2.69)	(0.88 to 1.66)	(0.81 to 1.58)	(0.61 to 1.16)
Isolite (n = 68)						
Geometric mean uBPA	0.48	0.47	0.76	0.64	0.38	0.63
95% CI	(0.35 to 0.66)	(0.33 to 0.67)	(0.48 to 1.22)	(0.42 to 0.96)	(0.27 to 0.52)	(0.45 to 0.87)
Ratio	Reference	Reference	1.60	1.34	0.79	1.32
95% CI			(0.98 to 2.61)	(0.85 to 2.12)	(0.53 to 1.18)	(0.86 to 2.03)
Other (n = 15)						
Geometric mean uBPA	0.50	0.32	0.90	0.60	0.59	0.68
95% CI	(0.22 to 1.16)	(0.16 to 0.64)	(0.35 to 2.33)	(0.25 to 1.46)	(0.24 to 1.46)	(0.31 to 1.52)
Ratio	Reference	Reference	2.28	1.52	1.50	1.74
95% CI			(0.76 to 6.87)	(0.66 to 3.54)	(0.49 to 4.59)	(0.59 to 5.15)
Characteristics of study visits and uBPA						
Time of posttreatment visits, median (IQR)	NA	NA	2 d (1 to 4)	1.1 wk (0.7 to 2.9)	4 wk (3 to 5)	16 wk (6 to 21)
Below the limit of detection, n (%)	100 (54)	89 (49)	73 (40)	89 (48)	104 (57)	101 (55)

All geometric mean values are ng/mL.

BisGMA, bisphenol A-glycidyl methacrylate; IQR, interquartile range; NA, not applicable; uBPA, urinary bisphenol A.

^aRange during which the study visit occurred.

Figure. Geometric mean urinary bisphenol A (uBPA) versus time since treatment.

our findings. Our findings were also similar when stratifying on potential confounders including demographics and consumption of canned foods. We did not study BPA from other dental materials (e.g., BPA dimethacrylate).

We do not know the extent of dental-related BPA exposure in pregnant women or their fetuses. BPA has known adverse health effects to fetuses, and dentists should consider conservative courses of therapy until dental-related BPA exposure in pregnancy is clarified (Yolton et al. 2011; Berger et al. 2018). BPA exposure in dental professionals who routinely handle bisGMA-based materials or products containing BPA (e.g., tubing for nitrous oxide) is unknown, and airborne exposure to BPA may occur (Fu and Kawamura 2010). Efforts to understand this potential occupational exposure is worth consideration.

In the largest cohort to examine dental-related BPA exposure, we found that children experience short-term, statistically significant increases in exposure to BPA. Increases in BPA from dental-related treatment return to baseline by 4 wk. When feasible, minimizing exposure in the course of dental treatment can help to reduce overall burden of BPA exposure in children and improve child health outcomes.

Author Contributions

C.M. McKinney, contributed to conception, design, data acquisition, and interpretation, drafted and critically revised the manuscript; B.G. Leroux, contributed to conception, design, data analysis, and interpretation, drafted and critically revised the manuscript; A.L. Seminario, A. Kim, contributed to conception,

design, data acquisition, and interpretation, critically revised the manuscript; Z. Liu, contributed to data acquisition and interpretation, critically revised the manuscript; S. Samy, contributed to data interpretation, critically revised the manuscript; S. Sathyanarayana, contributed to conception, design, and data interpretation, critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of the work.

Acknowledgments

We thank the participants and the University of Washington Center for Pediatric Dentistry for their participation and collaboration. This work was supported by National Institutes of Health, National Institute of Dental and Craniofacial Research, R01DE025229 and the National Center for Advancing Translational Sciences, UL1TR002319. The authors declare no potential conflicts of interest with respect to the authorship and/or publication of this article.

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