Is There a Risk of Harm or Toxicity in the Placement of Pit and Fissure Sealant Materials? A Systematic Review

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Contexte : On observe depuis quelque temps un intérêt croissant pour la question de la libération in vivo de composants des scellants dentaires, comme le bisphénol A (BPA), lequel peut se lier aux récepteurs des œstrogènes des cellules visées en des concentrations subtoxiques in vitro et nuire ainsi au développement, à la santé et à la reproduction des espèces fauniques. Le présent examen systématique avait pour but d'examiner si la mise en place d'agents de scellement pour puits et fissures cause une toxicité et a, de ce fait, des effets néfastes chez les patients.

Méthodologie : Une recherche documentaire d'articles pertinents (depuis les premiers relevés jusqu'à mars 2007) a été faite dans Ovid MEDLINE, CINAHL et d'autres bases de données bibliographiques.

Résultats : La recherche documentaire a permis de recenser au total 377 articles dont la pertinence a été évaluée à partir du titre et du sommaire. Onze études originales satisfaisaient aux critères d'inclusion. Ces articles ont été lus en intégralité et notés par 2 examinateurs indépendants.

Recommandations : Les données laissent croire que l'utilisation de scellants dentaires ne présente pas de risque d'exposition au BPA pour les patients. Cependant, afin de réduire – s'il en est – les risques de toxicité lié au BPA présent dans les scellants, les fournisseurs de soins dentaires devraient appliquer un léger abrasif (p. ex., une pierre ponce) à l'aide d'un applicateur coton ou d'une cupule à prophylaxie; demander aux enfants plus âgés et aux adolescents de se gargariser avec de l'eau tiède pendant 30 secondes ou encore laver la surface du scellant pendant 30 secondes avec une seringue air-eau tout en aspirant les liquides et les débris de la bouche de l'enfant.

Pour les citations, la version définitive de cet article est la version électronique : www.cda-adc.ca/jcda/vol-74/issue-2/179.html

Xenoestrogens, a group of chemicals that exert a biological reaction comparable to that of estrogens, bind to the estrogen receptors of relevant cells at subtoxic concentrations, impairing the development, health and reproductive systems of wildlife.[1,2] One of these substances, bisphenol A (2,2-bis[4-hydroxyphenyl]propane [BPA]), is produced by an acid-catalyzed reaction of phenol and acetone.[3] BPA is a plasticizer used in the manufacture of many types of products, including polycarbonate plastic food-storage containers and the epoxy resin used as the lacquer lining of autoclavable food or beverage cans.[4,5] In vitro studies have shown that BPA has the potential to bind to the estrogen receptor, activate estrogen-response elements and stimulate the growth of an estrogen-sensitive cell line.[6]

In dentistry, BPA is used in the synthesis of matrix monomers such as dimethacrylate monomers for dental composite resins and fissure sealants. BPA presents as an impurity in some resins (bisphenol A diglycidyl dimethacrylate [bis-GMA]) or as a degradation product in others (such as bisphenol A dimethacrylate [bis-DMA] and bis-GMA).[7]

In toxicology, the migration of oligomers, monomers, and the precursors of synthetic polymers and other low-weight molecules from polymer networks must be carefully controlled to avoid the harmful reaction of these molecules with biologically important molecules (for example, the formation of adducts by BPA and bisphenol A diglycidylether (BADGE) or the binding of BPA to the estrogen receptor).[8] Resin-based dental composites require in situ polymerization of monomers through a chemical curing process or photoactivation; however, because this process is not fully complete, some residual monomers may remain intact and can leach out of the cured resin into the surrounding media.[7,9] The dimethacrylate resin matrix of composite restorations in the oral cavity is exposed to the effect of different chemical and mechanical factors, and enzymatic hydrolysis of the ester linkage in a pendant methacrylate group produced by unspecific esterase and other enzymes in saliva.[2] All together, these factors may contribute to the breakdown of resin-based restorations and result in a slow and persistent degradation of the materials.[10]

Across Canada, sealants are part of mandatory preventive treatments that children have soon after the eruption of their first permanent molar. No Canadian nationwide data are available about the number of sealants placed through public health programs. The number placed by general practitioners is not known, but has been increasing, especially because sealants are a service covered by some health insurance plans. In Ontario, Locker and Matear[11] conducted a study of a stratified random sample of 55 schools located in 6 health unit or department areas in Ontario (Durham Region, York Region, City of Hamilton, Ottawa-Carleton, Thunder Bay and Simcoe County). In these schools, all students in junior kindergarten, senior kindergarten, and grades 2, 4, 6 and 8 were screened. Overall, of the 11,814 children screened, 2,734 had dental care needs. Based on an unweighted sample of 8,613 students and a weighted sample of 134,736, the authors found that 7.1% of the students were in need of sealant treatment. In a recent survey[12] of 7-year-old school children in Peel, 8.0% (n = 704) in 2001–2002 and 7.1% (n = 764) in 2004–2005 had dental sealants; in Brampton and Caledon, 6.7% (n = 1,047) of 7-year-old school children in 2005–2006 had dental sealants.

Recent increased use of composite restorative materials in modern dentistry has sparked increased interest in the in vivo release of dental sealant components. The purpose of this systematic review was to investigate whether the placement of pit and fissure sealant materials causes toxicity and thus harms patients.

Methods

Database Search

A search of the literature, from the earliest record up to March 2007, for relevant articles was done with Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily, Ovid MEDLINE, Ovid OLDMEDLINE, CINAHL (Cumulative Index to Nursing and Allied Health Literature), Evidence Based Medicine section of the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects, EMBASE, Health and Psychosocial Instruments, HealthSTAR/Ovid Healthstar, International Pharmaceutical Abstracts, and PubMed.

Search Strategy

The subject headings "harms" or "toxicity" or "bisphenol" (731,840 items) were combined with "sealant" (7,300 items) to identify articles that included these terms (685 items). After duplicates were removed, searches were limited to English publications (377 items). No other exclusion criteria were set at the initial stage to ensure all potentially relevant articles that included the search keywords were found. At each stage, both authors independently assessed the search strategy.

The titles of the 377 articles were reviewed by both authors. The abstracts of 44 of these articles were examined to identify full articles for complete assessment. Of those identified, articles that did not discuss the toxicity of dental sealants or provide background information (review articles) were excluded. The reference lists of these articles were searched to identify any other articles relevant to the research question. All of these cited articles were found in the original searches. All known guidelines and position statements were also retrieved.

Results

A total of 11 articles about the toxicity of dental sealants were selected for review.

Studies that Found No Significant Level of BPA

Rueggeberg and others[13] examined how effectively 6 surface treatments reduced the oxygen-inhibited layer of light-cured unfilled dental sealant (Delton Light Curing Pit & Fissure Sealant, Dentsply Ash, York, Penn.):

1. no treatment (the control treatment)
2. 20-second rinse with an air-water syringe spray
3. 20-second manual application of a dry cotton roll
4. 20-second manual application of a wet cotton roll
5. 20-second manual application of a water/pumice slurry with a cotton pellet
6. 20-second application of a water/pumice slurry with a prophy cup on a slow-speed handpiece.

The authors analyzed the amount of monomers (bis-GMA; triethylene glycol dimethacrylate [TEGDMA];

and bis-DMA) remaining after each treatment and found that the treatment that used pumice eliminated the greatest amount (93%–95% of the untreated control values) of any type of residual monomer. They suggested that clinicians can most effectively reduce patients' exposure to the uncured components in the oxygen-inhibited layer of sealants by using a mild abrasive, such as pumice, either on a cotton applicator or in a prophy cup.

Schafer and others[14] reported the proliferative effects of BPA and bis-DMA in cells with high levels of estrogen receptors. They did not detect BPA in American-made sealants and detected bis-DMA in only a few. They suggested that the surface layer of the sealant be treated to reduce the possibility of unpolymerized bis-DMA remaining on the tooth.

Sasaki and others[15] investigated the changes in the BPA concentration in saliva after restoration with 9 commercially available composite resins. They found that much less than 100 ng/mL of BPA were contained in the saliva after teeth were filled with composite resin, but that gargling with tepid water for 30 seconds can remove BPA from the oral cavity, making it an important risk-management technique.

Joskow and others[16] placed clinically appropriate amounts of either Helioseal F (Ivoclar Vivadent, Amherst, N.Y.) or Delton LC Opaque pit-and-fissure sealant (Dentsply/Ash) in 14 men and measured BPA in saliva and urine samples collected at prescribed intervals after the sealants were placed. Patients treated with Delton LC had significantly higher doses of BPA than those treated with Helioseal F. The authors found that Helioseal F leached negligible amounts of urinary and salivary BPA, amounts that were similar to baseline levels. Delton LC resulted in low-level exposure to BPA (at levels within the range at which estrogen receptor–mediated effects are seen in rodents). They concluded that placement of clinically relevant amounts of Delton LC sealant resulted in low-level exposure to BPA; however, exposure was negligible after placement of Helioseal F. They also suggested that saliva collection (e.g., by spitting or suctioning) after sealant placement likely reduces systemic absorption of BPA from dental sealants.

Fung and others[17] determined the rate and time course of BPA released from a dental sealant (Delton LC) when applied at a single 8-mg dose (1 tooth) or 32 mg (8 mg on each of 4 teeth) to the teeth of 40 healthy adults (18 men and 22 women, 20–55 years of age) who did not have histories of pit and fissure sealant placement or composite resin restorations. BPA was detectable in some saliva specimens collected at 1 hour and 3 hours; however, BPA was not detectable in the saliva samples beyond 3 hours or in any of the serum specimens. The authors concluded that BPA released orally from a dental sealant may not be absorbed or may be present in nondetectable amounts in systemic circulation.

Ortengren[18] assessed the water sorption and solubility of 6 proprietary composite resin materials and found no detectable quantities of BPA during the test period.

Nomura and others[19] tested 3 monomers (bis-GMA, urethane dimethacrylate and TEGDMA) and 5 polymerization initiators (camphorquinone, benzoyl peroxide, dimethyl para toluidine, 2-dimethylamino-ethyl-methacrylate and 1-allyl-2-thiourea) commonly used in dental composite resins for estrogenic activity and compared these with BPA. They found no estrogenic agonist activity for any of these 8 monomer and polymerization initiators.

In their in vitro study, Hamid and Hume[20] identified and quantified the major (or detectable) components released from 7 commercially available light-cured pit and fissure sealants using 10 extracted third molars. They found that the total amount of TEGDMA released was on the order of 0.25 mg per tooth in eluates from all sealants tested, and bis-GMA at much lower levels (about one thousand-fold less) in eluates from 1 sealant only. They found no BPA in any eluates.

Schmalz and others[21] chemically analyzed the BPA content of different fissure-sealant resin monomers and their release of BPA under hydrolytic conditions. They found that no BPA is released under physiologic conditions from fissure sealants based on bis-GMA if pure base monomers are used.

Studies that Found Detectable Levels of BPA

Quinlan and others[22] investigated the potential cytotoxicity of Spectrum composite resin (Dentsply, Surrey, U.K.) and Dyract AP compomer (Dentsply). They found that both materials can be potentially toxic, particularly if the degree of light cure is inadequate. Overall, apoptosis occurred when fully cured materials (40-second light-curing) were used, and necrosis occurred when partially cured materials (4-second light-curing) were used.

In a study of potential cytotoxic and mutagenic effects of dental composite materials (Solitaire and Solitaire 2, Heraeus Kulzer, N.Y.; Tetric Ceram, Ivoclar Vivadent, Liechtenstein; Dentsply, DeTrey, Germany; Definite, Degussa AG, Germany), Schweikl and others[23] ranked the cytotoxic effects of the composites according to 50% cell survival (EC50) values after a 24-hour exposure period as follows: Solitaire (most toxic) = Solitaire 2 < Tetric Ceram < Dyract AP < Definite (least toxic). The authors suggested that mutagenic components of biologically active composite resins should be replaced with more biocompatible substances to avoid health risks for patients and dental personnel.

Pulgar and others[8] studied biphenolic components eluted from 7 composites: Charisma (Heraeus Kulzer, Wehrheim, Germany), Pekalux (Bayern Leverkusen, Germany), Polofil (Voco, Cuxhaven, Germany), Silux-Plus (3M, St. Paul, Minn.), Z-100 (3M), Tetric (Ivoclar, Schaan, Liechtenstein), Brillant (Coltene Whaledent, Alstatten, Switzerland) and

1 sealant (Delton, Dentsply, York, Penn.) before and after in vitro polymerization. They found BPA, bis-DMA, bisphenol A diglycidylether, bis-GMA, and ethoxylate and propoxylate of bisphenol A in the media in which samples of different commercial products were maintained under controlled pH and temperature conditions. They confirmed the leaching of estrogenic monomers into the environment by bis-GMA-based composites and sealants at concentrations similar to those that have produced biologic effects in in vivo experimental models.

Nocca and others[24] evaluated the in vitro cytopathic effects of self-curing and light-curing orthodontic composite resins on the mouse fibroblast cell line using a cytotoxicity test. They found that the chemical-cured material they examined was more cytotoxic than the light-cured material.

Tell and others[25] examined the potential toxic effects of several orthodontic adhesives (Monolok [Rocky Mountain/Orthodontics, Denver, Colo.]), Unite [Unitek Corporation, Monrovia, Calif.], One to One [TP Laboratories Inc., La Porte, Ind.], Adaptic [Johnson & Johnson, New Brunswick, N.J.], Orthomite [Rocky Mountain/Orthodontics]) immediately after polymerization and at various time intervals up to 2 years after polymerization. They found that all materials tested showed cytotoxic effects immediately after polymerization and that the toxic effect decreased with time and after polymerization. However, even 2 years after the initial polymerization, toxicity was still evident in all adhesives but Orthomite.

Al-Hiyasat and others[26] investigated the cytotoxicity of 3 types of dental composites. Fifteen specimens of the composites (Admira, Voco; Feltik Z250, 3M; Tetric Ceram, Ivoclar Vivadent) and 15 specimens of their flowable derivatives (Admira Flow, Feltik Flow, Tetric Flow) were used to determine the compounds released from these materials. They found that Z250 and Tetric Ceram were less cytotoxic than their flowable derivatives. However, the Admira composite was significantly more cytotoxic than Admira Flow. Among the standard composites, Tetric Ceram was the least cytotoxic and Admira the most. Tetric Flow was the most cytotoxic and Admira Flow was significantly the least cytotoxic among the flowable materials tested. Bis-GMA and TEGDMA were found in the eluates of all the materials; urethane dimethacrylate was present in all eluates except the eluate of Feltik Flow. The authors concluded that flowable derivatives are more cytotoxic than traditional composites, whereas the ormocer Admira Flow is less cytotoxic than the Admira composite.

Conclusions and Recommendations

Our review of guidelines and position statements revealed concerns in the community about the release of BPA from plastics in general use. Dental concerns, however, are specific to sealants and composite restorations. Because the literature on this topic is extensive and complex, it merits a much larger review of all the issues around bis-GMA, including all dental concerns.

None of the dental sealants that carried the American Dental Association (ADA) Seal in 2007 released detectable BPA. These products were Helioseal Type II and Helioseal F Type II (Ivoclar-Vivadent Inc., Amherst, N.Y.), Seal-Rite Type II and Seal-Rite Low Viscosity Type II (Pulpdent Corp, Watertown, Mass.), and Conseal F (SDI North America Inc., Bensenville, Ill.). However, it should be noted that as of December 31, 2007, the ADA has phased out the Seal of Acceptance program for professional products and focuses instead on a product evaluation newsletter, the *ADA Professional Product Review* (PPR). As a result, the products listed above no longer carry the ADA Seal of Acceptance.[27] The ADA evaluated 9 pit and fissure sealants in the PPR for: a) setting time for glass ionomer sealants, b) depth of cure for external-energy-cured pit and fissure sealants, and c) polymerization shrinkage stress and polymerization stress rate for external-energy-cured pit and fissure sealants. The 9 products were: Aegis Pit & Fissure Sealant (Harry J. Bosworth Company, Skokie, Ill.), Guardian Seal (Kerr Corp, Orange, Calif.), Clinpro (3M ESPE, St. Paul, Minn.), Helioseal (Ivoclar Vivadent, Amherst, N.Y.), Delton Light Cure (Dentsply Professional, York, Penn.), Riva Protect (SDI North America Inc.), Embrace WetBond (Pulpdent Corp), UltraSeal XT Plus (Ultradent Products, South Jordan, Utah), and GC Fuji Triage (GC America Inc, Alsip, Ill.). This evaluation did not include testing for the release of BPA from these products.[28] However, in its recent ADA position and statement paper,[29] the ADA suggests that there is no cause for concern about potential exposure to BPA from composites or sealants at this time. Nevertheless, the ADA "…supports additional research into how much BPA people are actually exposed to and at what levels of exposure health effects start to occur."[29]

From these reviews, we summarize the overall findings about BPA. Fung and others[17] concluded that "BPA released orally from a dental sealant may not be absorbed or may be present in nondetectable amounts in systemic circulation." Schafer and others[14] suggest that "dentists should reassure parents that their children are less likely to be exposed to BPA from sealants than from the ingestion of soft drinks or canned food." Government regulatory agencies in Europe (the European Food Safety Authority), Japan and the United States (the American Food and Drug Administration) have concluded that human exposure to BPA from normal contact with food that is in contact with polycarbonate plastic is very low and poses no known risk to human health.[30–32]

Based on our review of literature, we recommend that dental providers avoid the potential for BPA toxicity from the dental sealants by treating the surface layer of the sealant to reduce the possibility of unpolymerized BPA remaining on the tooth. Following one of these procedures will accomplish this task:

- using a mild abrasive, such as pumice, either on a cotton applicator or with a prophy cup
- having older children and adolescents gargle with tepid water for 30 seconds
- washing the surface of the sealant for 30 seconds with an air-water syringe while suctioning fluids and debris from a child's mouth.

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