Bisphenol-A in Dental Composites

The presence of plastic polymers in dental composites has caused uncertainty in the minds of people who are suspicious of the potential impact of plastics on human health. In particular, one component of composite resins, bisphenol-A (BPA), has attracted attention because it can act as a xenoestrogen. For better or for worse, all dental materials are non-biological chemicals, and the only way we have to evaluate their safety is to use scientific risk assessment.

There is a good deal of literature now available comparing exposures with reference doses and toxic threshold data on BPA in its various uses. Two things stand out. First, dental manufacturers claim that there is no free, unreacted BPA in bis-GMA or bis-DMA resins. It would take heating to a temperature of several hundred degrees to liberate the BPA from these resins. Second, measurements of exposure to BPA from dental resins reveal potential doses that are hundreds or thousands of times less than any known toxic level. That's about as much reassurance as we can get, given the artificial nature of dental materials.

The following article is a review of the scientific literature on BPA in dental resins, reproduced by permission of the author, Steven G. Hentges, PhD. It is taken from this website: http://www.bisphenol-a.org/human/dental.html.
In addition to the references Dr. Hentges presents, the IAOMT sponsored a risk assessment for BPA by Dr. Mark Richardson, which was published as:

Richardson, G.M. 1997. Assessment of adult exposure and risks from components and degradation products of composite resin dental materials. Human and Ecological Risk Assessment, 3(4): 683-697.

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Summary

Dental sealants and composites play a significant role in preventing tooth decay and in maintaining dental health. Dental sealants are an important tool in preventing dental caries by providing a protective barrier on the teeth, particularly when used during a child's formative years. Dental composites are mainly used to fabricate tooth colored fillings and veneers as well as in the cementation of crowns. In addition to their functional and aesthetic properties, composites provide an alternative to mercury amalgam.

In 1996, Nicolas Olea and coworkers at the University of Granada in Spain reported detectable levels of bisphenol A (BPA) in the saliva of patients treated with dental sealants, suggesting that children receiving this treatment could be exposed to the chemical. These findings and the subsequent clinical recommendations made by the authors, stimulated public concern about this dental treatment. Subsequent studies, culminating with that of Eric Fung and coworkers, indicate that while extremely low levels of BPA can be detected in the saliva of individuals treated with selected dental resins in the hours immediately following application, no BPA was detected in the blood stream.

A review of key studies on dental resins containing BPA-based materials reveals that the highest reported acute oral exposure to BPA is more than 50,000 times lower than levels shown to cause acute oral toxicity in animal studies. Although repeated exposure to BPA from dental resins is not expected to occur, the highest reported acute oral exposure is also below the maximum acceptable or "reference" dose for BPA, which is set for repeated exposure over a lifetime. Consequently, exposure to BPA from dental resins for both adults and children is minimal and poses no known risk to human health.

For additional information, see the statement from the American Dental Association and a summary of a study from the Journal of the American Dental Association.

Background

Dental composites are complex mixtures of materials that generally consist of an organic resin matrix, reinforcing inorganic filler and a silane-coupling agent, which connects the filler and the resin matrix. Sometimes known as "white filling" or "synthetic porcelain", composites are commonly used as a tooth-colored restorative material, for example in the fabrication of fillings and veneers, and the cementation of crowns. Composites without

the filler and coupling agent are commonly used as sealants, which effectively isolate pits and fissures to help prevent caries in adults and children.

Composite resins are formulated from a mixture of monomers and are most commonly based on bisphenol A glycidyl methacrylate, usually abbreviated as bis-GMA and sometimes known as Bowen's monomer after it's inventor. Because of the new treatment options made available, bis-GMA based composites are considered to be one of the most significant innovations of modern dentistry.

In addition to bis-GMA, composite resins generally include other monomers to modify the properties of the resin, for example bisphenol A dimethacrylate (bis-DMA), ethylene glycol dimethacrylate (EGDMA) and triethylene glycol dimethacrylate (TEGDMA). Although several key components of composite resins are derived from BPA, there is no known use of BPA itself in composite resins.

Composites and sealants are provided and applied in the form of a paste or viscous liquid, which is then cured or hardened after application by polymerization of the resin with a UV or visible light treatment. In addition to monomers and fillers, composites also may contain initiators, to promote polymerization from light treatment, and stabilizers, to maximize storage of the uncured resin and stability of the cured resin. (Soderholm and Mariotti, 1999; Guertsen, 1998).

Is Bisphenol A Released from Dental Composites and Sealants?

Several researchers have studied whether BPA leaches from cured dental composites or sealants. In 1996, Nicolas Olea and coworkers at the University of Granada (Spain) and Tufts University in Boston, MA applied a commercially available sealant to twelve molars each of eighteen men and women, using about 50 mg of sealant per person. Saliva samples were collected one hour prior to and one hour after application. After treatment, all saliva samples were reported to contain BPA in amounts ranging from 90 to 931 µg (3.3 to 30 ppm). (Olea *et al*, 1996)

In a similar study, Arenholt-Bindslev and coworkers applied two commercially available sealants to four molars of four men per sealant. Saliva samples were collected before and immediately after application, as well as one and twenty-four hours after application. The only saliva samples reported to contain BPA were those collected immediately after application of one of the sealants, which was the same sealant studied by Olea. The level of BPA reported ranged from 0.3 to 2.8 ppm, which is approximately 10 times lower than the amount of BPA reported by Olea. No BPA was found in the saliva samples collected at one and twenty-four hours after application of this sealant or in any of the saliva samples collected after application of the other sealant, with a 0.1 ppm limit of detection. (Arenholt-Bindslev *et al*, 1999)

In a third larger study, Fung and coworkers at the University of Nebraska applied the same sealant studied by Olea and Arenholt-Bindslev to the teeth of eighteen men and twenty-two women. Half of the subjects received 8 mg of sealant applied to one tooth while the other half received 32 mg of sealant applied to four teeth. Both saliva and blood samples were collected before application of the sealant as well as at intervals of one, three and twenty-four hours, and three and five days after application. Some, but not all, of the saliva samples collected at one and three hours after application were found to contain BPA in the range of 5.8 to 105.6 ppb. No BPA was found in saliva samples collected after twenty-four hours or in any of the blood samples, in both cases with a detection limit of 5 ppb. The maximum level of BPA detected was more than 250 times lower than the maximum amount reported by Olea. (Fung *et al*, 2000)

Based on the data reported in the three studies involving application of sealant to teeth, it appears that low levels of BPA may be released from certain sealants, although only during a short time period immediately after application of the sealant. Further, no detectable levels of BPA have been found in blood after application of a sealant that releases low levels of BPA into saliva.

Although a wide range of BPA levels have been reported in saliva, the validity of the high levels reported by Olea has been questioned. The analytical method used by Olea may not have been capable of distinguishing between BPA and TEGDMA, which is known to be a predominant component released from dental sealants but not reported at all by Olea. The maximum amount of BPA that could reasonably be released from the dental sealant has been estimated to be less than the lowest level reported by Olea. Consequently, TEGDMA may have been misidentified as BPA in the Olea study (Atkinson *et al*, 2002). Additional complicating factors may have been the excessively large amount of sealant applied per subject in the Olea study, potentially resulting in incomplete polymerization and higher leachability (Fung *et al*, 2000).

The validity of the lower levels of BPA reported by Fung and Arenholt-Bindslev is supported by *in vitro* leachability studies on cured dental sealants. Nathanson and coworkers at Boston University tested the leachability of seven dental sealants that were cured in glass dishes. None of the seven sealants showed detectable amounts of BPA after extracting with ethanol with a detection limit of 0.0001 µg BPA/mg sealant (Nathanson *et al*, 1997). Similarly, Hamid and Hume tested the leachability in water of seven dental sealants that were applied to extracted teeth or stainless steel molds and cured. None of the seven sealants showed detectable amounts of BPA (Hamid and Hume, 1997). In a later study from Olea's laboratory, samples of composites and sealants polymerized in glass dishes were extracted with water of varying pH for twenty-four hours. Low levels of BPA (< 1 µg BPA/mg sealant) were reported for these materials (Pulgar *et al*, 2000). Although these studies may not be fully predictive of sealant leachability *in vivo*, since they do not consider potentially important factors such as mastication or the effect of salivary enzymes, they do suggest that high levels of BPA are not expected.

What is the Source of BPA in Dental Sealants?

Dental sealants typically contain monomers that are derived from BPA, such as bis-GMA and bis-DMA, but there is no known use of BPA itself in dental sealants. Since it is known that these monomers may leach from dental sealants, the stability of the monomers has been studied under a variety of conditions, including in saliva, to determine if they may hydrolyze to form BPA. Bis-GMA, the base monomer for many composite resins, has been found to be stable to various hydrolytic conditions (Schmalz *et al*, 1999). However, two researchers have reported that bis-DMA is hydrolyzed to BPA, which likely accounts for the BPA detected in extracts from certain sealants (Schmalz *et al*, 1999; Atkinson *et al*, 2002).

Potential Exposure and Margin of Safety

The highest amount of BPA reported in saliva by Olea, 931 µg, forms the basis for the calculation of potential exposure and margin of safety. This quantity was reported in saliva after the application of one brand of dental sealant in one individual in a single study. Further studies by other researchers have reported much lower levels of BPA and have suggested that BPA may have been misidentified in the Olea study due to interferences in the analytical method. In addition, no detectable amounts of BPA were found in the blood, indicating that while some BPA may leach into saliva, systemic exposure does not occur.

Assumptions:

1. 931 µg (0.931 mg) of BPA in saliva. This is a very conservative assumption since it is the highest value found in the literature. This value is still the highest even if one assumes that 100% of bis-DMA converts to BPA.

2. Average weight of a child is 25 kg (55 pounds).

3. Exposure subsides in the hours immediately following application. No BPA was detected in samples after three hours.

Since exposure to BPA from dental sealants occurs only in a short time period immediately after the sealant is applied, and dental sealants are applied only very infrequently, safety is most appropriately evaluated as an acute exposure event. In laboratory animals, BPA has been found to have very low acute oral toxicity, with LD50 values greater than 2000 milligrams per kilogram of body weight.

In comparison, the potential exposure to BPA from use of dental sealants on a child of average weight, based on the assumptions above, is 0.037 milligrams per kilogram of body weight. This exposure level is more than 50,000 times lower than the LD50 values that have been reported for BPA. As noted, actual exposure to BPA from dental sealants

is most likely well below the highest reported value, which further increases the margin of safety.

These assumptions also indicate that exposure to BPA is less than the maximum acceptable or "reference" dose of 0.05 milligrams per kilogram of body weight per day (US EPA, 1993). The EPA reference dose is set for a lifelong daily intake of a substance and includes a considerable safety margin for sensitive stages of life such as childhood. Although exposure to BPA from dental sealants would not occur daily for a lifetime, this comparison further indicates that even the worst-case exposure to BPA from dental sealants represents no harm.

The reference dose for BPA has recently been confirmed by a three-generation study in rats (Tyl et al, 2002), which found no adverse effects on reproduction from BPA at doses of 50 milligrams per kilogram body weight per day and lower. The US EPA calculated the reference dose by dividing the Lowest-Observed-Adverse-Effect-Level (LOAEL, 50 milligrams per kilogram body weight per day) from an earlier chronic toxicity study by an uncertainty factor of 1000. Applying that same uncertainty factor to the No-Observed-Adverse-Effect-Level (NOAEL, 50 milligrams per kilogram body weight per day) from the Tyl study confirms the safety of the reference dose, 0.05 milligrams BPA per kilogram body weight per day. Since the maximum estimate of BPA exposure from dental sealants is less than the reference dose, human exposure to BPA from dental sealants is minimal and poses no known health risk.

Conclusions

Small amounts of BPA may leach from dental sealants immediately after application of the sealants to teeth. No BPA has been detected in blood samples, indicating that there is no detectable systemic exposure to BPA from dental sealants.

- The source of BPA that leaches from dental sealants is likely to be from hydrolysis of bis-DMA, a common monomer used in dental resin formulations.
- When evaluated as an acute exposure event, the highest level of BPA reported in saliva from dental sealants is more than 50,000 times lower than the LD50 values that have been reported for BPA.
- Although BPA exposure from dental sealants does not occur daily throughout a lifetime, the highest level of BPA reported is also below the maximum acceptable or "reference" dose for BPA of 0.05 mg/kg body weight/day.
- A recent three-generation study has confirmed the safety of the maximum acceptable or "reference" dose for BPA of 0.05 mg/kg body weight/ day.
- Consequently, human exposure to BPA from dental resins is minimal and poses no known health risk.

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