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Case Report Open Access

# Dysfunctional Uterine Bleeding Following Treatment with Bisphenol-A Glycidyl Methacrylate (BisGMA) Dental Resins

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## Abstract

**Objective:** Bisphenol-A (BPA) is a xenoestrogen used in many consumer products. Here we present a case of dysfunctional uterine bleeding after exposure to dental sealant containing BPA.

**Design:** Case Report

**Setting:** Academic Medical Center

**Patient:** A 32-year-old presenting with uterine bleeding.

**Intervention:** Dysfunctional uterine bleeding was diagnosed, and no therapy was initiated.

**Results:** The patient continued to experience bleeding following each exposure.

**Conclusion:** Female patients undergoing dental procedures that use BPA containing compounds may experience dysfunctional bleeding.

**Keywords:** Bisphenol A; BPA; Endocrine disruptor; Xenoestrogen; Dysfunctional uterine bleeding; Dental sealants; Dental resins

## Introduction

Bisphenol-A (BPA) is an endocrine disrupting chemical affecting reproduction and fertility [1]. It is found in epoxy resins that line cans, polycarbonate plastics, and dental sealants. Exposure to BPA occurs as it leaches from these materials, and has become nearly ubiquitous; ninety five percent of Americans have urine BPA levels that are equal to or are above concentrations associated with adverse reproductive outcomes in animal models [1,2]. Therefore, it is important to identify potential sources of human exposure as well as potential health consequences.

The reproductive effects of BPA are due to its estrogenic activity, which is mediated by its binding to estrogen receptor alpha and beta [1]. BPA is association with estrogen related pathologies such as endometriosis and endometrial cancer [1-4]. Other estrogen related pathologies, particularly dysfunctional uterine bleeding, may also be associated with the weak estrogenic effects of BPA.

Dental sealants contain a mixture of monomers derived from BPA. These sealants are primarily comprised of Bisphenol-A glycidyl methacrylate (bis-GMA); however some sealants contain monomers such as ethylene glycol dimethacrylate (EGDMA), triethylene glycol dimethacrylate (TEGDMA) and Bisphenol-A dimethacrylate (bis-DMA). EGDMA and TEGDMA are non-BPA co-monomers released by the dental resin. Bis-DMA is hydrolyzed to BPA by salivary enzymes, while Bis-GMA, is thought to remain stable under hydrolytic conditions, yet its risk warrants further investigation [5-7]. The use of BPA containing compounds during dental procedures may pose reproductive and gynecological risks; therefore these materials must be further investigated particularly focusing on potential BPA release from polymers and the extent of human exposure.

Here we present a case of BPA exposure followed by dysfunctional uterine bleeding, likely due to the estrogenic effects of BPA.

## Case Report

A 32-year-old gravida-0 para-0 underwent a dental procedure that included nine dental fillings (23 surfaces) in one treatment, three weeks after her last menstrual period. Three days later she experienced heavy bleeding and dysmenorrhea. The bleeding began five days prior to her next expected menstrual period therefore she was originally not alarmed. The patient presented to her gynecologist office three weeks later complaining that the dysmenorrhea and bleeding have not subsided. She described the bleeding as heavier than usual with intermittent days of spotting followed by resumed bleeding that required twice as many pad changes daily and often the use of two pads simultaneously [8].

Menarche occurred at age 12 and the patient described her typical menses as regular-occurring every 28 days and lasting for 5-6 days. The patient had no history of irregular bleeding. Her past medical history was non-contributory with the exception of seasonal allergies controlled by Loratadine, migraines controlled by zolmitriptan, and

untreated depression. She is a chronic smoking with a 15 pack year history, drinks alcohol occasionally, and smokes marijuana. She does not use any recreational or illicit drugs [9]. She has no history of surgeries or hospitalization. Both of her parents are alive and well. She has never been married and has no children or siblings.

The pelvic exam revealed a normally sized uterus with no anomalies except for blood in the vagina. A pelvic sonogram found the uterus with no evidence of fibroids or other pathology [10]. The ovaries appeared normal bilaterally. Small follicles were seen in both ovaries and traces of free fluid were present in the cul-de-sac. Laboratory findings included white blood cells 6,100/uL, red blood cells 4.96 x 106/uL, hemoglobin 13.9 g/dL, hematocrit 42.3%, mean corpuscular volume 85.2 fL, platelets 256,000/uL, and hCG 0.0 UA/mL. The bleeding time, prothrombin time, activated partial prothrombin time, and the international normalized ratio were within normal range. The level of FSH was 12.6 IU/L and LH 8.1 IU/L. The results of liver function tests and thyroid function tests were within normal range as were the levels of prolactin, and dehydroepiandrosterone sulfate (DHEAS). The patient was diagnosed with dysfunctional uterine bleeding. Uterine bleeding continued for another three weeks and then resolved. Ten days later the patient returned to her dentist for another dental filling. The following day she began to bleed heavily, however, the bleeding resolved after forty-eight hours [11].

## Discussion

In animal studies, exposure to BPA has been associated with disrupted ovarian development, ovarian cyst-adenomas, induction of mammary gland ductal hyperplasia and mammary carcinoma *in situ*. As we previously described, BPA alters progesterone receptor expression in the nonhuman primate. Similarly, studies in human cells have shown that the monomer bis-GMA increases progesterone receptor expression, as well as mammary gland epithelial cell yields, and MCF7 breast cancer cell proliferation [12].

Exposure to BPA is not limited to dental sealants. BPA is also found in shatter-proof plastic products made of polycarbonate plastic which include baby bottles, water bottles, and food storage containers. It is also found in the plastic lining of canned foods as well as the internal coating of metal food and beverage cans. BPA can leach from these products if they are exposed to harsh detergents, acidic liquids, or high temperature liquids [13].

There is no known use of unpolymerized BPA in dental sealants, however, monomers such as bis-GMA and bis-DMA are derived from BPA. BPA in the saliva of patients treated with dental sealants results from the presence of esterase, a salivary hydrolase that can break ester linkages releasing BPA. Varying levels of BPA found in the saliva of patients treated with these sealants was primarily associated with bis-DMA and not bis-GMA. When the ester linkages of the bis-DMA molecule are hydrolyzed, BPA can be generated, likely accounting for the BPA detected. The amount of BPA ranges from low to significant; significant being less than or equal to 2 ppm. One study found up to 80% of bis-DMA in saliva was converted to BPA, and 82% converted when subjected to esterase. The amount of BPA detected in saliva drops after three hours, suggesting it may be metabolized or absorbed by the body [14].

The patient reported here was treated with dental sealants containing bis-GMA. The stability of bis-GMA in various hydrolytic conditions remains unclear as there are conflicting studies regarding the release BPA from bis-GMA in the presence of esterase. Further research is warranted to see whether human exposure to BPA from bis-GMA based dental sealants results from a mechanism distinct from that which breaks down bis-DMA, namely, hydrolysis by salivary enzymes. Though bis-GMA has yet to conclusively show the release of BPA in esterase, the estrogenic effects of bis-GMA are well-documented and could potentially lead to estrogen-related pathologies, including abnormal uterine bleeding. Once the composite resins are degraded, a significant portion can be swallowed and absorbed by the intestine. Absorption of BPA by the intestine may lead to a variety of long-term health effects, which need to be further investigated. Given the endocrine disrupting effects of BPA and the findings presented here, exposure to BPA containing dental sealants should be considered as a potential cause of dysfunctional uterine bleeding.

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