ORIGINAL SCIENTIFIC ARTICLE

Does Urinary Bisphenol-A Change after Bariatric Surgery?

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BACKGROUND: One of the world's highest volume chemicals is bisphenol-A (BPA), an organic compound with a high solubility in fat. An emerging body of literature has suggested a link between BPA, obesity, and insulin resistance. The study aim was to determine if surgical weight loss is associated with changes in BPA levels.

STUDY DESIGN: Demographic, preoperative, and 3-, 6-, and 12-month postoperative urine and laboratory data were prospectively collected on 22 bariatric surgery patients at a single academic institution. Laboratory values included hemoglobin A1C, fasting insulin, and fasting glucose. Demographic, preoperative and postoperative data, and urinary BPA levels were compared using Student's *t*-tests and simple regression analyses using GraphPad Prisim6 software.

RESULTS: Patients were predominantly privately insured (86%), female (83%), and white (68%). Urinary BPA excretion was negatively correlated with weight at 6 months ($r = -0.47$, $p = 0.029$) and 12 months ($r = -0.65$, $p = 0.006$). The average weight before surgery was 274 pounds. Average preoperative BPA excretion was 2.4 ng/mL (SD = 1.0 ng/mL) in patients lighter than average weight and 1.3 ng/mL (SD = 0.7 ng/mL) in patients heavier than average weight ($p = 0.006$). Average BPA excretion at 12 months was 2.5 ng/mL (SD = 2.2 ng/mL) among lighter patients and 0.58 ng/mL (SD = 0.4 ng/mL) among heavier patients ($p = 0.05$). Follow-up included 18 patients at 3 months, 22 patients at 6 months, and 16 patients at 12 months. Higher urinary excretion of BPA preoperatively correlated with lower 6-month patient weight ($r = -0.557$, $p = 0.025$). Higher preoperative fasting insulin correlated significantly with reduced BPA excretion at 6 months postoperatively ($r = -0.5366$, $p = 0.032$).

CONCLUSIONS: Excretion of BPA increases as bariatric surgery patients lose weight. Heavier patients with insulin resistance may store more BPA in adipose tissue and therefore excrete less BPA. (J Am Coll Surg 2018;■:1−6. Published by Elsevier Inc. on behalf of the American College of Surgeons.)

Morbid obesity is the leading public health crisis of the industrialized world, and it affects men and women of all races and socioeconomic status.[1-3] Today, two-thirds of US adults are overweight, and one-half of adults are obese.[4] Severe obesity reduces life expectancy by 5 to 20 years.[5] It is predicted that the current generation will have a shorter life expectancy than the previous generation.[5,6]

One of the world's highest volume chemicals is bisphenol-A (BPA), an organic compound with a high solubility in fat.[7,8] An emerging body of literature has suggested a link between BPA and obesity.[8-10] Several studies in animal models[8,11,12] have shown that low doses of BPA during the perinatal period of development result in an increase in body weight throughout life. Further studies[13,14] have also shown that BPA exposure preceding puberty increases body weight in rats. It has been suggested that the mechanism for this weight gain is acceleration of differentiation of adipose tissues.[15] In these studies, it has been presumed that increases in body weight were due to increases in body fat, although the change in body fat after BPA exposure has yet to be studied. Studies in mice have also shown BPA has to lead to increases in glucose intolerance and insulin resistance.[16]

On a cellular level, studies have demonstrated changes in gene expression from even low doses of BPA.[17,18]

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Marmugi and colleagues[17] showed that low doses of BPA affected genes involved in lipid synthesis in mice. This study showed a dose-response relationship between BPA levels and lipogenesis, suggesting that even low levels of BPA can increase de novo fatty acid synthesis. Similarly, Hugo and associates[18] showed that low doses of BPA suppressed adiponectin release. Decreased levels of adiponectin have been associated with increased risk for metabolic syndrome. Together, these studies suggest that low levels of BPA, which could reasonably be found by environmental contaminants, can effect cellular regulation related to obesity.

More recent studies have looked at BPA in humans. Levels of BPA have been correlated with generalized obesity, abdominal obesity, and insulin resistance in middle aged and elderly adults.[8] In a cross-sectional analysis of urinary BPA concentration from the National Health and Nutrition Examination Surveys (NHANES), Carwile and Michels[19] demonstrated a relationship between BPA and obesity. Individuals in this study with higher levels of BPA were more likely to be classified as obese and have abdominal obesity, which is often used synonymously as excess fat. Epidemiologically, BPA has also been associated with obesity in children, independent of other risk factors.[20,21] These cross-sectional studies using the NHANES data[19-21] suggest that BPA may be an emerging obesogenic risk factor.

Studies have also reported associations between BPA concentrations and coronary artery disease, myocardial infarction, angina, and diabetes.[22-24] It is important to note that all studies to date in humans have been cross-sectional in design and have yet to show a direct relationship between changes in excess fat and BPA levels.

No studies have yet examined whether a change in weight results in a change in BPA level. Bariatric surgery remains the only effective and enduring treatment for morbid obesity. Since 1997, bariatric surgery in the US has grown significantly as mounting evidence proves the safety and efficacy of current surgical procedures.[25] Patients who undergo bariatric surgery typically lose 40% excess fat, a consistent finding in the literature.[26] This predictable weight loss provides a mechanism to study the relationship between weight loss and changes in BPA levels. Bariatric surgery will allow for the examination of whether BPA levels are predictive of weight loss.

In addition to weight loss, bariatric surgery has been widely successful in improving type 2 diabetes mellitus in 4 of 5 patients. The surgery has also been shown to reduce the risk of heart failure and various cancers.[27,28] Because some evidence suggests a correlation between BPA levels and the same comorbidities resolved by bariatric surgery, bariatric surgery also provides a mechanism to examine the resolution of these conditions as it relates to excess fat loss and BPA level changes.

Because BPA is a ubiquitous chemical, it is crucial to understand how rapid weight loss, as occurs after bariatric surgery, is related to changes in BPA levels. This is the first study of its kind to prospectively examine changes in BPA levels before and after weight loss surgery. Because BPA is stored in fat, we hypothesized that the rapid weight loss that occurs during the first 6 months after bariatric surgery will be associated with rapid excretion of BPA in the urine as fat is shed from patients' bodies. Further, we hypothesized that a relationship will be seen between initial BPA levels and weight loss postoperatively because high BPA levels would be expected to be correlated with more changes in lipogenic gene expression, so these patients would have a more difficult time losing weight postoperatively.

Given the widespread use of BPA in plastic bottles and food containers, this study has widespread implications for understanding and treating obesity and changes in BPA levels after rapid weight loss. This study provides the first comprehensive, prospective examination of BPA levels after bariatric surgery and weight loss.

METHODS

Twenty-two morbidly obese patients undergoing bariatric surgery at a single academic institution were prospectively enrolled at their preoperative clinic visit. All patients qualified for surgery based on the 1991 National Institutes of Health consensus criteria. Twelve of the patients (55%) underwent Roux-en-Y gastric bypass, 8 underwent sleeve gastrectomy (36%), and 2 underwent laparoscopic adjustable gastric banding (9%). All Roux-en-Y gastric bypass, sleeve gastrectomy, and laparoscopic adjustable gastric banding procedures were performed by an experienced (>2,500 cases) surgeon.

Demographic data were collected before surgery, including weight, BMI, age, race, and type of insurance. The BMI was calculated as weight in kilograms divided by height in meters squared. To follow changes in BMI over time, percentage of excess weight loss (EWL) was calculated as: 100 × current weight loss/(preoperatively body weight − ideal body weight). Laboratory values included, but were not limited to, hemoglobin A1C, fasting insulin, and fasting glucose, and were measured before and at 3, 6, and 12 months after operation. All patients were given the same dietary and exercise instructions.

Urine samples were collected preoperatively and at 3, 6, and 12 months postoperatively for BPA analysis. Urinary BPA analyses were completed by NMS labs and involved adding isotopically labeled (D16) internal standard to