



ENDOCRINE DISRUPTORS: BISPHENOL A AND ITS RELATION WITH OBESITY

*Lucas Wanderley Rodrigues
Gonçalves de Sá¹,
Luciano Nunes de Sousa²,
Thyciara Fontenele Marques³,
Gabriel Pereira Bernardo⁴,
Lorena Pereira Bernardo⁵,
Lucas Leimig Telles Parente⁶,
Rodrigo Emmanuel Leimig
Telles Parente⁷,
Maria Valéria Leimig Telles⁸,
Djailson Ricardo Malheiro⁹*

Abstract: The prevalence of obesity is, worldwide, in wide intensification. This increase stimulates the search for new hypotheses that explain the genesis of the metabolic syndrome. This article seeks to clarify the obesogenic hypothesis of bisphenol A (BPA), based on its endocrine disrupting potential. Methodology: For the development of the present study, the Scopus and PubMed databases were used, from descriptors generated by the DeCS: Endocrine Disruptors; Foods; Obesity; Bisphenol A and its correspondents in English. Randomized and controlled trials were considered eligible, focusing on publications in English and Portuguese. The survey was conducted on April 11, 2017, with publications of the last five years being leaked. Based on this, 87 articles were obtained and, from the reading of the title and its abstracts, 26 publications were selected. After the complete reading of the 26 articles selected, 18 articles were obtained that served as a basis for this bibliographic review. Bisphenol A appears as an important agent that causes obesity in the contemporary world, interfering in the signaling mechanism of the endocrine system, being its high exposure linked to many of the habits present in the current context. Conclusion: Based on the possible consequences of bisphenol A, the reduction of human exposure to the compound should be considered. Based on this, alternatives to BPA in the production of industrial plastic polymers have to be considered since increased exposure to the endocrine disruptor is closely related to industrial production.

Keywords: Endocrine Disruptors, Obesity, Bisphenol A

¹ Medical student at the Faculty of Medicine Estácio of Juazeiro do Norte, Brazil. Contact: lucaswanderley10@hotmail.com;

² Medical student at the Faculty of Medicine Estácio of Juazeiro do Norte, Brazil. Contact: desousaluciano@outlook.com;

³ Faculty of Medicine Estácio of Juazeiro do Norte, Brazil.. Contact: thyciarafontenele@gmail.com;

⁴ Medical student at the Faculty of Medicine Estácio of Juazeiro do Norte, gabrielpbernardo@hotmail.com;

⁵ Medical student at the Faculty of Medicine Estácio of Juazeiro do Norte, lorenapbernardo@hotmail.com;

⁶ Medical student at the Faculty of Medicine Estácio of Juazeiro do Norte, parente_lucas@hotmail.com;

⁷ Medical student at the Faculty of Medicine Estácio of Juazeiro do Norte, rodrigo.parente.leimig@hotmail.com;

⁸ Ph.D., Professor at the Faculty of Medicine Estácio of Juazeiro do Norte, valerialeimigtelles@hotmail.com;

⁹ Faculty of Medicine Estácio of Juazeiro do Norte, Brazil.. Contact: djailsonricardo@gmail.com.

Introduction

Obesity today is considered a pandemic. This is not a recent phenomenon, but a consequence of the change of habits of the people caused mainly after the Industrial Revolutions. Food production and consumption were influenced in order to meet the political-economic needs of large companies. However, economic interests were more valued to the detriment of the health of the population, due to large-scale production, generally do not meet nutritional needs. With this, the pathologies related to food intake, among them obesity, have affected the population more intensely.

Although obesity is commonly related to sedentary lifestyle, high calorie diets and genetic factors, these are not the only factors that influence the pathology. Excess food consumption and inadequate physical activity are the major risk factors for obesity, but they do not fully explain the pathophysiology of the disease (Schneider; Brozek; Keen-Rhinehart, 2014). In addition to lifestyle factors, environmental chemicals act as endocrine disrupters, playing a favorable role in the development of adiposity (Chevalier; Fenichel, 2015).

The endocrine system is a set of glands that act on the secretion of hormones that maintain body metabolism. However, this system may undergo changes by the action of various substances, called endocrine disrupting compounds (EDCs). This nomenclature is used to define a diverse class of synthetic and natural compounds that have the ability to alter various components of the endocrine system, inducing adverse health effects in exposed individuals (Vom Saal, et al., 2012).

An example of an endocrine disruptor is bisphenol A, a chemical widely used worldwide in the production of plastic polymers (Vafeiadi, et al., 2015). Recent epidemiological and animal studies have suggested that exposure to BPA may influence the development of obesity and related pathologies, such as type 2 diabetes, cardiovascular diseases and liver diseases (Marmugi, et al., 2014; Khalil et al., 2014). Human exposure to BPA is ubiquitous at low levels, and occurs mainly through migration from pesticides and food and beverage containers (Furt, Hoepker, Francis, 2017).

The present study was produced as a result of the dissemination and updating of the data, in 2017, through Vigitel 2016, about overweight and obesity in Brazil by the Ministry of Health. Vigitel warns about Brazilian health by monitoring the frequency and distribution of the main risk factors for chronic noncommunicable diseases, describing the annual evolution

of the indicators. Thus, the data disclosed showed the marked evolution of overweight in the Brazilian population. This information influenced the production of the above, arousing the interest about the factors involved in adipogenesis. Based on this, other potentially obesogenic conditions were investigated, as well as unbalanced diet, sedentary lifestyle and genetic factors explaining the exposure to Bisphenol A and its possible implications on the pathophysiology of obesity.

Methods

For the development of the present study, the Scopus and PubMed databases were used, from descriptors generated by the Decs: Endocrine Disruptors; Foods; Obesity; Bisphenol A and its correspondents in English. Randomized and controlled trials were considered eligible, focusing on publications in English and Portuguese. The survey was conducted on April 11, 2017, being filtered publications of the last five years. Based on this, 87 articles were obtained and from the reading of the title and its abstracts, 26 publications were selected. After the initial filtering, the full reading of the 26 selected articles began and 18 articles were obtained which served as basis for this literature review.

We included papers that presented relevant studies on endocrine disruptors focusing on bisphenol A and its influence on the pathophysiology of obesity. It excluded from the research, in addition to the results in duplicate, studies that addressed, not to mention bisphenol A and obesity, other endocrine disruptors and pathologies.

Results

Overweight and obesity in Brazil

Obesity is a chronic metabolic disease present throughout the globalized world, its prevalence tends to grow more and more, especially in the industrialized world. Brazil is no exception to this rule. Being an industrialized nation and adhering to Western customs, habits of the great developed powers, mainly of the United States, were incorporated into Brazil. As

a result, the production, distribution and consumption of food in the country was adapted to the market demands and the diseases caused by poor diet, such as obesity, grew substantially. Thus, several studies seek to quantify and update the data on obesity in Brazil, in order to understand its etiology in order to provide data necessary for guidelines to combat the disease to be fixed.

Data recently published by the Ministry of Health, through Vigitel 2016 (Graph 1), show the evolution of overweight in the Brazilian population:

Graph 1: Data on the growth of overweight rates among men and women in Brazil, gathered in 2016, through the Vigitel and published in April 2017 by the Ministry of Health.

The parameter used to determine excess weight in the research was the Body Mass Index (BMI), which classifies the individual in terms of weight, but is also widely used as an indicator of health risk, having relationships with several metabolic complications (Brazil, 2016). The BMI value is obtained by the ratio of the mass of the individual in kilograms to the height in meters squared. Based on this, reference values are used to classify the population as to the distribution of their body mass: an individual is overweight when his BMI value is equal to or greater than 25 kg / m². Obesity is diagnosed when the BMI is equal to or greater than 30 kg / m² (Who, 2000).

According to Graph 1, overweight affects more than half of the population interviewed, being more frequent among men. The average of the genres grew 26.3% in ten years, going from 42.6% in 2006 to 53.8% in 2016 (Brazil, 2016). The greater prevalence of overweight among the male population can be explained by the fact that it is common among men to neglect healthy habits. However, this is not the only explanation for such a phenomenon. In addition to the sociological point of view, there is the biological one, which reports sexual differentiation as an important factor influencing adiposity. Among the peculiar characteristics of each genus are: body weight, adipose tissue distribution and hormonal action (Schneider; Brozek; Keen-rhinehart, 2014), which may suffer changes due to substances in the environment considered to be deregulatory of the endocrine system, such as Bisphenol A.

The Ministry of Health also updated data on obesity in the country. According to Graph 2, obesity rates among men and women have grown over the years, reaching 18.9% of the Brazilian population (Brazil, 2016). These data concern both the government and the Brazilians, considering that obesity can affect in various pathological conditions such as cardiovascular disease and type 2 diabetes (Marmugi, et al., 2014).

Graph 2: Data on the growth of obesity rates among men and women in Brazil, collected in 2016, through Vigitel, and published in April 2017 by the Ministry of Health. Moreover, these data support a global trend to overweight, a fact that worries the international health agencies. This reflects the growing demand, by researchers for evidence to explain the pathophysiology of obesity. Based on this, new hypotheses are created and tested all the time. Thus, the obesogenic hypothesis of endocrine disrupting substances emerges as a new path to be explored by the scientific community, presenting promising studies on the subject.

Discussion

A brief introduction to endocrine disrupting substances

Chemicals that disrupt the endocrine system are released into the environment in different ways. They are mainly used in packaging industries, pesticides and food constituents. Clinical evidence, experimental models and epidemiological studies suggest that EDCs pose great risks for humans, affecting different organs and systems. Multiple mechanisms are involved in the direction of the normal system via estrogen receptors, nuclear receptors and activation of steroid receptors (maqbool, et al., 2016). The disruption of endocrine signaling systems by EDCs is the central issue for the discussion of the potential of endocrine disrupting substances to disrupt metabolic processes and eventually lead to obesity (Vom Saal, et al., 2012).

Based on this, the investigation of the various endocrine disrupting compounds is necessary to seek new aetiological explanations about the pathophysiology of obesity. Thus, multiple studies discuss the various endocrine disruptors found in the environment and their possible clinical and pathological repercussions. However, due to the abundant variety of EDCs, then consider this study is one of the main and most studied class of compounds: bisphenol A.

The Bisphenol A in the pathophysiology of obesity

Most people are exposed daily by consuming foods and beverages in which BPA is leached from polycarbonate containers, including bottles and refillable bottles (Chevalier; Fenichel, 2015; Barraza, 2012). In cross-sectional studies, it was demonstrated that prolonged exposure to low doses of BPA affects the differentiation of adipocytes, by increasing the pre-adipocyte growth regulatory genes altering the adipogenesis. It was also observed higher accumulation of lipids in mature adipocytes (Ariemma, et al., 2016).

However, it is important to consider the possible variables in achieving these results. Its influence may vary according to the study population and its physiological characteristics, such as gender, distribution of adipose tissue and age (Schneider; Brozek; Keen-Rhinehart, 2014). However, BPA, through early interference, can increase both the number of adipocytes and the lipid content, since it is capable of affecting the growth of preadipocytic cells in both genders (Ariemma, et al., 2016).

However, bisphenol A does not always reflected clinically equitably among the study populations. Therefore, understanding the natural process of sexual differentiation has been fundamental for understanding the effects of endocrine disrupters on the development of the sexually dimorphic reproductive system. As the energetic balance traits are sexually diverse, understanding sexual differentiation is likely to be critical for understanding the effects of endocrine disruptors on energy balance (Schneider; Brozek; Keen-Rhinehart, 2014).

Thus, epidemiological evidence reinforces the obesogenic capacity of BPA in restricted study groups, such as in animal test populations, demonstrating that exposure to BPA for 8 months in adult animals results in metabolic disturbances consisting of increased adipose tissue mass, hyperglycemia, glucose intolerance, and increased liver cholesterol biosynthesis. (Marmugi, et al., 2014). On the other hand, the association between urinary levels of bisphenol A and overweight among girls aged 9 to 12 years has been proposed in specific human populations, anticipating the development of puberty and promoting weight gain during this period (LI, et al., 2013).

Another perspective proposes the relationship of Bisphenol A with high levels of glucose in the blood of animals without any increase in insulin levels (Marmugi, et al., 2014). In addition, it was suggested that insulin resistance is directly associated with BPA concentrations in urine (Valentino, et al., 2016) and, from tests with obese children, similar conclusions were obtained (Menale, et al. 2016). Thus, in addition to the exposure to bisphenol A, which has an influence on obesity, indirectly influencing the diagnosis of

diabetes, it may also act directly on insulin resistance and increase plasma glucose. This is in line with the studies of Chevalier; Fenichel, (2015), who suggested the potential of BPA in negatively affecting metabolic homeostasis and aggravate or accelerate the development of obesity, metabolic syndrome and type 2 diabetes in individuals at risk.

In addition, numerous studies reflect on the obesogenic hypothesis of bisphenol A in relation to exposure during pregnancy. Results suggest that exposure to prenatal BPA is associated with increased total body fat and central adiposity (Hoepner, et al., 2016). BPA as a lipophilic compound, may accumulate in adipose tissue during fetal life, affecting health in adulthood, through adverse effects on organ and tissue growth and development (Valentino, et al., 2016). The susceptibility of fetal development to the potential adverse effects of BPA can be obtained through the analysis of biomarkers of fetal metabolic function such as leptin and adiponectin (Ashley-Martin, et al., 2014).

As diet is the main source of BPA, it is possible that overweight people consume more products containing it than normal weight individuals, which results in higher urinary concentrations of bisphenol A (Harley, et al., 2013) . Thus, the analysis should be done with caution, since the occurrence of obesity varies according to the food source, and diet is a factor that promotes variations in obtaining the results.

Study groups that were exposed to BPA may present an increase in adiposity, but the disruptor will not always be the main factor in this condition, playing a secondary role in the development of obesity. For example, overweight individuals may consume soft drinks, canned foods, or processed foods, which are relevant sources of BPA, but this can not be the only cause of obesity, but a by-product of dietary habits associated with the disease (Harley et al. 2013).

Therefore, in view of this clear association between obesity and other components of the metabolic syndrome, with human exposure to bisphenol A, it is essential that national and international regulatory bodies carefully analyze their possible threats to the health of the population. Also, in relation to other endocrine disrupting substances, considering that, predominantly, EDCs act together and not individually (Biemann; Fischer; Santos, 2014). Therefore, studies aim to investigate not only bisphenol A, but also other substances considered to be disrupting the endocrine system and its potential effects on the body, seeking to standardize the screening system for possibly obese patients (Fernandes, et al., 2013).

Conclusions

The extensive literature produced on the clinical effects of Bisphenol A serve as basis for possible cautious steps in relation to population exposure to the endocrine disruptor. Thus, alternatives to BPA as much as the other EDCs should be considered, so that people's health is preserved and industrial production does not have significant impacts.

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