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The influence of bisphenol A on the human body

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Introduction: Bisphenol A (BPA) is a substance commonly used in industry for the production of everyday plastic products. It is also found in thermal paper. Global pollution of the environment by BPA results in constant exposure to its harmful effects. This substance penetrates the skin, respiratory tract and food into the body. BPA, due to its structure similar to estrogens, disturbs e.g. functioning of the endocrine system and increases the risk of certain cancers.

Material and methods: The PubMed and Google Scholar databases were used to review the literature.

Description of knowledge: Exposure of breast cancer cells to BPA results in increased aromatase synthesis and increased proliferation of ER + cells. Moreover, BPA stimulates the growth of neoplastic breast cancer cells not only at high doses but also at low doses (<25 μg / kg / day). This substance has an affinity for the estrogen receptor. Daily doses of BPA have been found to increase the density of the mammary gland in mammography. Exposure of this substance to human prostate epithelial cells induced the potential of cancer development in prostate cells. Recent studies have shown that BPA causes increased bronchial reactivity and reduced epidermal regeneration capacity, which proves its pro-inflammatory effect. Research proves that BPA reduces the ability to learn and disrupts the Glu / GABA neurotransmitter ratio.

Conclusions: The ubiquitous presence of BPA has a negative effect on living organisms. By accumulating in adipose tissue, it exposes us to constant exposure, which is dangerous even in low doses. Increases the risk of infertility and cancer. Acting pro-inflammatory, it increases the susceptibility to allergens. There are calls for the use of BPA-free packaging and for steps to be taken to reduce BPA production.

Key words: bisphenol A; BPA; estrogen; mechanisms; receptors; cancer.

Introduction

Bisphenol A (BPA) is a substance that is widely used in the consumer industry. It is most often used in the form of a monomer in the production of epoxy resins, polycarbonate plastics, and also as an additive to eliminate excess hydrochloric acid in the production of polyvinyl chloride (PVC). [1] BPA occurs in plastic products such as food containers, toys, inner coating of cans. Its annual production was estimated in 2016. for about 8 billion tons. People who work with thermal paper on a daily basis are at serious risk. [2] Particularly high BPA is found in bottled beverages. [3] Importantly, significant amounts are also found in fresh produce such as fruit and vegetables. It is related to irrigation of crops with polluted water [4]. The main route of exposure is oral, inhalation through inhalation of house dust, and transdermal route. Maternal-fetal transfer is also possible. [5,6] This compound can be released from plastics during the production, use and disposal of the product. It has been proven that high temperature and variable pH favor the release of BPA from plastics. An additional factor contributing to the accumulation of the compound in the environment is the presence of high levels of sodium chloride or vegetable oils. [7]

Research suggests that when rapidly absorbed orally, BPA is conjugated with glucuronic acid in the liver. Such a combination ensures stability and lipophilicity of the compound, thanks to which it is easily accumulated in various parts of the body. [8] Due to its affinity for adipose tissue, BPA may increase the risk of obesity by stimulating adipogenesis, causing the accumulation of lipids in adipose tissue and increasing the level of cytokines.

Over the years, attention has been paid to the impact of BPA on the endocrine system, which is why the production of baby bottles and food packaging free of this substance was initiated. However, substitutes such as bisphenol AF (BPAF), bisphenol S (BPS), bisphenol F (BPF), bisphenol B (BPB), bisphenol AP (BPAP), bisphenol E (BPE) and bisphenol Z (BPZ) likely have similar toxicity to original relationship. [9] In contrast, syringarezinol has been characterized as a safer alternative to BPA in the production of epoxy resins, which gives hope for a gradual withdrawal of BPA from the market. [10] Exposure to BPA is projected to continue to increase, therefore it is imperative to identify potential effects on the human body. Already in the 1930s, it was found that BPA affects estrogen receptors in analogy to female sex hormones. [11] Moreover, it has been proven that this compound can cause anti-estrogenic activity by competing with endogenous 17-beta estradiol, which results in the blockade of the estrogenic response. [12] Effects on estrogen receptors may increase the risk of breast cancer. [13]. It is worth adding that BPA is a potential factor causing uterine cancer [14], ovary [15], liver [16], testes [17] and prostate [18], acting not only in toxic doses, but also in low doses that simulate the concentration of BPA in the environment. [19] Studies also show that the substance in question may have anti-androgenic effects by direct binding to androgen receptors [20]. An important aspect is also a significant effect on the thyroid receptors. This compound may interfere with the synthesis and secretion of thyroid hormones [21]. Importantly, some studies have shown that higher BPA levels are detected in children compared to adults [22].

Material and method

The PubMed database and Google Scholar were used to review the literature. You searched for articles in English using the following keywords: BPA, bisphenol A, estrogen, mechanisms, receptors, cancer.

Description of knowledge

The most thoroughly analyzed aspect of the influence of BPA on the human body is the activity analogous to estrogens. As we know, high estrogen increases the risk of breast cancer. BPA mimics these hormones by stimulating estrogen receptors, causing excessive cell proliferation. This compound regulates various processes, e.g. cell migration and apoptosis, leading to neoplastic changes. Taking into account genetic mechanisms, BPA performs its functions through many oncogenic pathways, such as the STAT3, PI3K / AKT and MAPK pathways [23].

There is a positive correlation between exposure to BPA and an increased risk of breast cancer. Sprague et al. found a significant relationship between serum BPA levels and breast density in mammography in postmenopausal women. It was found that the mammographic density of the breast increased from 12% to 17% when the serum BPA concentration increased from undetectable to 0.55 ng / ml [24]. As is well known, mammographic breast density is an independent positive risk factor for breast cancer [25].

Statistically, a 5-10% increase in breast cancer risk occurs with a 5% increase in mammographic density.

Research shows that BPA causes uterine cancer as well as ovarian abnormalities. Newbold RR. et al. conducted a study in an animal model in which one group of mice was administered BPA dissolved in corn oil, while the control group was administered the oil alone without impurities. At 18 months of age, the reproductive system was examined. It turned out that there was an increase in the number of cystic ovaries and endometrial hyperplasia. Additionally, severe uterine pathologies such as leiomyomas, atypical hyperplasia and stromal polyps were noted. In all individuals from the BPA-exposed group, peri-ovarian cysts and progressive proliferation in the fallopian tubes were observed. [14]

Polycystic ovary syndrome is an increasingly common problem in the 21st century. Animal studies by Marina Fernández et al. have shown that exposure of newborns to BPA may increase the risk of this syndrome. Female rats exposed to BPA had increased serum testosterone and estradiol levels and altered GnRH secretion in adulthood. Conclusions have been drawn that exposure to high doses of BPA during brain development alters the functioning of the hypothalamic-pituitary-gonadal axis. This effect can be linked to the pathogenesis of polycystic ovary syndrome, however, studies to confirm this effect in humans and to identify toxic doses are needed. [15] Another disease that may be a potential cause of infertility is endometriosis. Higher BPA concentration has been observed among women struggling with endometriosis [26].

Gail S. Prins et al. have shown that exposure to bisphenol A early in life changes the sensitivity of prostate cells to hormones, increasing the risk of cancer formation later in life. The conducted study on human cells showed that exposure to BPA causes an increased incidence of intraepithelial neoplasia compared to the control group. It has been concluded that human prostate stem cells are direct targets for BPA and that developmental exposure to low dose BPA increases the risk of hormone-dependent cancer in human prostate epithelium [18].

A documented effect on BPA-induced carcinogenesis is a study by Manjunath K Nanjapp et al. Scientists tested male rats, which they divided into two groups. Increased proliferative activity of testicular cells was observed in the group that was exposed to BPA. After 10 days of starting the test, testosterone levels were close to zero, indicating destruction of Leydig cells. However, after 28 days there was a rapid recovery of this cell population as indicated by the high level of androgens. No such relationship was observed in the control group. In addition, attention has been paid to the increased expression of mitogenic regulatory proteins. [17]

As you know, the main route of BPA entering the body is through the alimentary tract. The liver is the first organ that receives blood along with the substances absorbed from the intestine. It turns out that BPA can induce tumor formation in the liver, as confirmed by Caren Weinhouse et al. A dose-dependent incidence of liver tumors was found in 10-month-old mice exposed to BPA. Among the tested animals as much as 23% had liver tumors or pre-neoplastic lesions [16].

An important aspect is the anti-androgenic activity of BPA. Studies show that this compound is able to compete with 5α-dihydrotestosterone (DHT) for the androgen receptor.

José-Manuel Molina-Molina et al. demonstrated that both BPA and its substitutes (BPS, BPF), after binding to the receptor, induce gene expression and cell proliferation specific for a given tissue. [20] Other studies suggest that BPA may also bind at several sites on the surface of the androgen receptor through hydrophobic bonds. [27]

Another example conducted on animals was the study by Asad Ullah et al. Male rats were exposed to various concentrations of BPA and its analogues for 28 days. The induction of antioxidant enzyme activity and an increase in markers of oxidative stress were observed. At the same time, a significant decrease in testosterone levels was noticed compared to the control group. This is evidence of damage to male gamete cells [28]. It is worth adding that BPA also affects female reproduction, because it has been observed to affect the development of ovaries, embryos and the quality of gametes [29].

Maternal exposure to BPA may influence spermatogenesis in the offspring, as has been demonstrated in animal studies. In juveniles, reduced sperm production and the height of the epithelium of the seminiferous tubules have been demonstrated. In addition, morphologically abnormal sperm were observed more often, with a reduced number of mitochondria and reduced acrosome and cell membrane integrity. These phenomena were accompanied by a slow sperm movement. [30] This study highlights the possible reduction in male fertility as a result of exposure to BPA.

The developing organism is particularly vulnerable to the negative effects of exposure to bisphenol A. Zhang H et al. conducted a study in which they investigated the effects of BPA on female mice. The study assessed the degree of development of the nervous system of the F1 and F2 offspring. It turned out that even a small environmental dose impaired learning and memory in male F1 mice. Moreover, maternal exposure to BPA decreased the number of neurons and the density of cells in the hippocampus. This feature was passed down from generation to generation. The neurotoxic effects were gender-dependent. Maternal exposure to BPA also led to changes in the levels of neurotransmitters in the hippocampus in F1 offspring. Overall, this study highlights the susceptibility of the development of the nervous system to BPA exposure at key times [31].

Nowadays, more and more people suffer from allergies. There have been many publications explaining this phenomenon, incl. hygiene theory. By examining the effects of BPA and the mouse model, scientists found that chronic systemic BPA challenge caused an allergic airway reaction to previously harmless ovalbumin. The influence of other substances has been eliminated. Moreover, in in vitro cultures, BPA significantly inhibited the proliferation of epithelial cells, resulting in impaired wound healing. Additionally, this substance promoted the expression of the cytokine TSLP. In vivo, BPA significantly induced systemic inflammation as the levels of inflammatory mediators in the skin, intestines and respiratory system increased [32]. A similar study was conducted in which an exacerbation of allergy to egg proteins was observed as a result of exposure to BPA. The symptoms appeared as an exacerbation of inflammation in the lungs. It has been proved that the mechanism of the inflammatory reaction was associated with the activation of the autophagy pathway by lowering mTOR expression [33]. Scientists emphasize the fact that further research is needed to confirm the positive effect of BPA on the induction of inflammation and inducing allergies.

Obesity and overweight is one of the major problems of the 21st century. Research has shown that exposure to BPA at an early age can be associated with many metabolic disorders.

It has been observed that among young patients there are positive correlations between exposure to BPA and obesity, increased percentage of body fat, high body mass index and abdominal circumference [34].

Conclusions:

The presence of bisphenol A and its derivatives is inevitable in our world. This substance can be found everywhere on earth, so it is important to determine its effect on the body. The studies outlined above clearly say that BPA increases the risk of some organ cancers such as the ovary, uterus, liver, testicle, prostate, and breast. The greatest dependence was observed in hormone-dependent neoplasms, due to the proven analogous action to sex hormones. Polycystic ovary syndrome, which can cause infertility, can also be caused by the presence of BPA in the body. A generalized inflammatory reaction and increased bronchial responsiveness to previously indifferent allergens - this is another effect of the influence of bisphenol A on humans. More attention should be paid to the neurotoxic effects of maternal BPA exposure on offspring as changes can be passed down from generation to generation. With regard to humans, a reduction in the ability to concentrate, memory skills can cause learning problems, so research should be carried out to finally investigate the effects of BPA on the nervous system. It is recommended to stop using plastic bottles and avoid heating food in plastic food containers. It is important to raise awareness among people about the potential effects of bisphenol A on the body and to influence the authorities to minimize the production of consecutive portions of BPA and its derivatives.

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