Does bisphenol A increase the risk of death?

Results of a study on the industrial chemical are not reliable from the point of view of the German Federal Institute for Risk Assessment (BfR)

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The industrial chemical bisphenol A is mainly used as a raw material for the production of polycarbonate plastics and synthetic resins. Due to its hazardous properties, it is subject to extensive legal regulations in Europe. In addition to the effects described so far, bisphenol A (BPA) is said to increase the risk of death according to a recently published study. From the point of view of the German Federal Institute for Risk Assessment (BfR), this conclusion has not been adequately proven.

The study by Wei Bao (University of Iowa, Iowa City) and his team, published in the journal "JAMA Network Open", investigated the question of whether exposure to BPA, determined by the BPA content in urine, and mortality are related. Data from a questionnaire and a urine sample tested for BPA from 3883 people in the USA were collected from 2003 to 2008 and linked to mortality data observed up to 2015. After considering possible influencing factors such as age, sex, ethnicity, diet and physical activity, there was a statistically noticeable (significant) increase in mortality in the group with the highest BPA content in the urine compared to the group with little BPA in their urine within the average observation period of about ten years.

According to the BfR, however, this study does not provide any conclusive evidence of a connection between exposure to BPA and an increased risk of death. Rather, the study design and the uncertainties caused by potentially existing further confounders call into question the validity of the investigation. The BfR therefore does not consider the results of this study to be scientifically proven.

In a cohort study, Bao et al. (2020) investigateda possible relationship between the uptake (exposure) of BPA and mortality over a mean observation period of about ten years in adults in the USA. To investigate this connection, the data of the study participants (including age, sex and BPA concentrations in the urine) collected once during a health examination between 2003 and 2008 were linked with information from the national mortality database and statistically analysed. On the basis of the BPA concentration in the analysed urine sample, the study participants were divided into three groups of roughly the same size (terciles with low, medium and high BPA concentrations in the urine).

After taking into account known influencing factors such as age, sex, ethnicity, diet and physical activity, a statistically significant increase in overall mortality of the group with higher exposure compared to the lower exposure group was shown over an observation period of approximately ten years. When only considering deaths due to cardiovascular disease and cancer, there were no statistically significant differences in mortality.

According to the BfR's assesment, this study does not provide convincing scientific evidence of a causal relationship between BPA exposure and increased mortality. The main points of criticism are listed below.

BPA concentration: One-time measurement not sufficient

Since the BPA content in urine was only determined once, no information on changes in the exposure status over time was available. In the study, the BPA concentration was used to divide into groups with low, medium and high BPA exposure. However, it is questionable to what extent this one-off measurement actually allows statements to be made about a person's BPA exposure over a longer period of time, so that one must assume an erroneous group assignment.

BPA is metabolised relatively quickly by the body after ingestion (mainly through food) and excreted through the kidneys. When BPA is metabolised, it loses its harmful properties. Another study (Ye et al., 2011) had previously shown that the BPA concentration in the urine of a single person can fluctuate widely over the course of the day. The fluctuation in the BPA concentration in individual urine samples from a single person over the course of the day is significantly greater (in some cases by more than ten times) than the variability in 24-hour urine samples collected from different people. For the study by Bao et al. (2020), one urine sample was used from each of the persons examined. Sampling was not carried out uniformly at the same time of day, but distributed throughout the day. The BPA concentration measured in a single spontaneous urine sample is therefore not very meaningful for a person's long-term exposure (based on the observation period to determine the mortality of about 10 years).

The authors point out this weakness, but rely on the statement by Ye et al. (2011), according to which individual BPA measurements can be used to estimate the population mean value (i.e. the mean concentration of BPA in the urine of the population). However, the population mean is not the decisive parameter for an event time analysis (determination of the time after which a certain event occurs) to estimate the mortality risk. This requires knowledge or at least an estimate of the long-term individual BPA intake and exposure.

Statistical evaluation with high uncertainties

The total number of deaths determined was 344 out of 3883 persons (this corresponds to 8.9%). Looking at the specific causes of death, 71 cardiovascular-related deaths and 75 cancer-related deaths were identified. The vast majority of deaths (198) are not classified further. Due to the relatively low total number of deaths for meaningful statistics and the low number of cardiovascular and cancer-related deaths, the uncertainties of the effect estimates are high, although the total population is relatively large. The observed correlations between the BPA concentration and mortality are therefore to be regarded as descriptive, but not statistically reliable.

In an observational study like the one by Bao et al. (2020) many different factors can interfere with the estimation of a (causal) relationship (“confounder”). Therefore, it is essential to take these into account in the study design and in the statistical analysis. The interpretation of the study results depends on the confounders included in the statistical evaluation. The authors do not justify their selection of potential confounders, which makes it difficult to interpret the study results in terms of a causal relationship.

Conclusion of the BfR on the study

The results published by Bao et al. (2020) on the relationship between BPA exposure and an increased mortality risk are subject to considerable uncertainties. These concern both the reliability of the exposure assessment and the statistical evaluation.

According to the BfR, the study does not show a confirmed causal relationship between BPA exposure and increased mortality. The study design and the uncertainties presented fundamentally call into question the significance of the study.

Legal regulations on BPA

Various hazardous properties have been identified for BPA (e.g. reprotoxic propertieskidney-damaging effects, hormone-like effects). Since 2016, BPA has been classified as toxic to reproduction in European chemicals legislation, and in 2017 and 2018 it was identified as a Substance of Very High Concern (SVHC) under the REACH Regulation due to its toxic and hormonal effects on human health and the environment.

The assessment of the European Food Safety Authority (EFSA) confirms that BPA can have endocrine-disrupting effects through various mechanisms, i.e. it can affect hormone levels in the body. EFSA classifies potentially harmful effects of BPA on the nervous, metabolic, immune and cardiovascular systems or mutagenic and carcinogenic effects as “less likely”. However, if the provisionally specified tolerable daily intake (temporary TDI) of 4 µg/kg body weight per day is adhered to, BPA is not assumed to pose any adverse health effects. In its exposure assessment from 2015, EFSA estimated the daily intake at a maximum of 1.5 µg/kg body weight per day. According to new data, it is now likely to be significantly lower.

The European Commission has banned BPA in thermal papers such as shop receipts since the beginning of 2020. BPA is also regulated in children's toys: For toys that are intended for children under 36 months of age or for toys that are intended to have contact with the mouth, a lower release limit value has been stipulated (0.04 mg/l based on test methods EN 71-10:2005 and EN 71-11:2005). This limit was chosen so that the amount of BPA that can be ingested through toys does not exceed 10% of the temporary TDI.

In addition the use of BPA for baby bottles made from polycarbonate was banned throughout the EU as early as 2011 as a precautionary measure. In 2018, the ban was extended to all drinking vessels and bottles made of polycarbonate for infants and toddlers in 2018. For all other food contact materials made of plastic, a limit value of 0.05 mg/kg has been set for the transfer of BPA into food. Further restrictions on uses in consumer products are planned.

Literature

Bao W., Liu B., Rong S., Dai S.Y., Trasande L., and Lehmler H.-J. (2020): Association Between Bisphenol A Exposure and Risk of All-Cause and Cause-Specific Mortality in US Adults. JAMA Network Open 3 (8), e2011620-e2011620. DOI: 10.1001/jamanetworkopen.2020.11620 (last accessed 9/2/2020)

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of Environmental Research and Public Health 11 (8), 8399-8413. DOI: 10.3390/ijerph110808399

About the BfR

The German Federal Institute for Risk Assessment (BfR) is a scientifically independent institution within the portfolio of the Federal Ministry of Food and Agriculture (BMEL) in Germany. It advises the German federal government and German federal states (“Laender”) on questions of food, chemical and product safety. The BfR conducts its own research on topics that are closely linked to its assessment tasks.

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