German Federal Institute for Risk Assessment

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Do microplastic particles increase the risk for a stroke?

The BfR has assessed a study on micro- and nanoplastics in deposits (plaque) in blood vessels.

An Italian research group detected micro- and nanoplastic particles (MNP) in the plaque in blood vessels (Marfella et al. [New England Magazine, 2024 Mar 7;390(10):900-910; doi: 10.1056/NEJMoa2309822]). Plaque samples from patients' inner carotid arteries that showed a narrowing of the blood vessels were investigated. These vessels supply the brain with blood. The plaque samples were investigated for the presence of MNP. The material type and amount of the detected particles were identified in the next step.

Based on the investigations, the patients were divided into two groups depending on whether MNP were detectable in the plaque or not. These two groups of people were examined for differences in regard to various physiological and molecular-biological aspects. Around three years after the samples were taken, a follow-up investigation took place which focused on whether and how many of the patients had died from a heart attack or stroke in this time period. The group whose plaque contained MNP fundamentally showed more pronounced disease progression (more heart attacks and strokes, including fatal ones, as well as higher inflammation parameters) than the group in which no MNP was found.

However, the study only describes correlations and no causation, i.e., a simple link is made between the presence of MNP in the plaque of the vessels and the diseases of the patients. It is not clarified as to whether the identified polyethylene (PE) and polyvinylchloride (PVC) particles cause plaque formation and inflammation of the vessel walls. Whether and how MNPs contribute to plaque formation is also not addressed. Furthermore, the study makes no statements regarding how the MNP enter the blood or the deposits.

The German Federal Institute for Risk Assessment (BfR) thus concludes that while the study describes a link, it does not show causality and does not contribute any evidence that MNP increases the risk for vessel diseases and resulting heart

attacks or strokes. In addition some scientific questions were identified which require closer scrutiny.

Assessment of the study

The basics

To the extent that this can be derived from the published material, the BfR is of the opinion that the study appears to have been well planned, implemented and analysed. The reporting followed the STROBE guidelines (https://www.strobe-statement.org/). Limitations were noted and discussed in the text. The study is primarily relevant for older people. It could be that some confounders were not considered during the analysis, which was also addressed by the authors. It is thus possible for expert readers to categorise the results and draw conclusions. One aspect deserving of criticism is that a comparatively sweeping statement is often initially made, with the relativisation and classification only becoming clear after closer reading. This potentially makes it difficult for people who are not at all or only cursorily versed in the scientific field to understand and interpret the study.

Design of the study

Plaque samples from people with circulatory diseases were investigated in the study. In all cases, therefore, the study involves patients (i.e., ill people, even if asymptomatic). There is not a “healthy” control group without plaque. It was a blind study, which can be considered positive, and the study-related limitations are clearly stated. Diseases were registered within a certain limited observational period.

The assignment of patients to one of the two groups took place depending on whether MNP was present in the deposits (plaque) in blood vessels. This does not necessarily mean, however, that people in which no MNP was detected actually had no particles at all in their plaque.

The study is an observational study and creates correlations between MNP and effects. This means that the study does not describe any causal context, which is also clearly stated. Sometimes, the authors attempt to calculate incidences from the available data.

Analytics and particle quantification

There is no universal analytical process for detecting MNP in tissues which is internationally scientifically recognised. The selected destructive processes are suitable for quantifying partial elements of MNP but do not provide information about the MNP’s size and nature. In contrast, spectroscopic processes do permit assertions regarding distribution and localisation, but they do not deliver a quantitative statement. The present study attempted to work with a combination of the best measurement methods currently available. A process was selected which is in alignment with current scientific knowledge. This also involves the evaluation of the raw data obtained.

Since every selected analytical method was checked by a second, independent process, it is likely that MNP was correctly identified during the study. The different measurable and non-

measurable size ranges were stated and explained. It was likewise clearly stated that contaminations (e.g., from the air, during sample preparations) cannot be ruled out.

Direct correlation of the results from qualitative and quantitative analysis methods for MNP is not possible in this type of study. It would, however, have been desirable for there to have been a classification of whether the qualitative and quantitative results of the analysis plausibly suit each other. This only took place in part.

Interpretation of the results and correlation with health parameters

The presence and accumulation of plastics in fat-rich structures of the body such as arterial plaque appears to be possible in pathophysiological terms. A causal context, i.e. that for instance the presence of MNP has an influence on plaque formation or the occurrence of cardiovascular diseases, cannot be established with the study. Mechanisms of action or molecular events that are required for plaque to form are not the object of the study. The study does not permit any assertions regarding possible MNP sources and routes of exposure. It is possible there are different confounders that could have influenced the results of the study.

Open questions requiring closer scrutiny

Several important scientific questions were not addressed by the study and require closer consideration. Plaque was examined for a number of different materials. All the examined plastic materials are most likely to be MNP. It remains unclear why only two materials (polyethylene and polyvinyl chloride) could be detected as usually a number of different polymers are found when it comes to MNP particles. Further, the limits of quantification of the used analysis methods remain undefined. A possible interpretation is that the MNP does not come from everyday contamination sources close to the consumer, and instead there was an exposure connected to a medical treatment, e.g., via injections or infusions. This possibility was, however, not mentioned in the study. The following points to such a cause: the age of the patient population, the fact that the detected polymers are those most used in medical applications, and that the detected particles are currently too large for it to be likely that they entered via plausible transport mechanisms via other body barriers (specifically intestine, lungs). Moreover, it seems very questionable that such a commonly occurring contaminant such as microplastic (to which likely all test persons were exposed in some way) could not be detected in the plaque of all test persons. It seems possible that MNP, provided it is systemically bioavailable, is absorbed by immune system cells which are specialised in fighting structures foreign to the body. The patients with a worse prognosis also showed overwhelmingly more inflammation in the plaque, i.e., an increased migration of immune cells into the investigated areas. MNP, then, could enter the plaque via the immune cells that infiltrate these areas when inflamed and bring MNP with them. The negative correlation between the detected MNP and the amount of collagen is striking. A mechanistic investigation of the causes underlying this would be useful.

Furthermore, there is a significant need for development and validation in regard to the analytical methods used. A larger body of reliable reference materials would be helpful. Using standard addition methods it would, in principle, be possible to further improve instrumental-analytical processes.

Plausibility of microplastics exposure via various exposure pathways

Fundamentally, the mere detection of microplastics does not allow for specific assertions regarding possible exposure routes into the body. In the case of the patients in the above study, exposure via products used in intensive medicine (e.g., infusion cannulas, catheters) appears conceivable and plausible. The study involves patients who already have a long history of illness. Therefore plastic particles, particularly PE and PVC, could directly enter the bloodstream via a corresponding vascular puncture.

The presence of microplastics in food has been shown in a number of studies. An intake of MNP via food is thus, in principle, conceivable. Particle size is the biggest factor for the MNP's entrance through the intestinal barrier. This also corresponds to the assessment of the European Food Safety Authority (EFSA) from 2016 which states that the transport of plastic particles via the intestine is predominately dependent on their size. Particles bigger than 1.5 micrometres (µm) cannot pass the intestinal barrier, meaning they are not systemically bioavailable (CONTAM-Panel 2016, https://www.efsa.europa.eu/de/efsajournal/pub/4501). This also corresponds to the latest scientific knowledge.

Further information about microplastics on the BfR website

Questions and answers on microplastics: Facts, research, and open questions
https://www.bfr.bund.de/en/microplastics__facts__research_and_open_questions-192775.html

BfR overview of microplastics
https://www.bfr.bund.de/de/a-z_index/mikroplastik-192184.html#fragment-2

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. The BfR advises the Federal Government and the States ('Laender') on questions of food, chemicals and product safety. The BfR conducts independent research on topics that are closely linked to its assessment tasks.

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