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Therapeutic apheresis: A promising method to remove microplastics?

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Microplastics and nanoplastics have emerged as a major and growing health concern, with recent data revealing alarming levels of human exposure and contamination. Thus, there is a clear and urgent need for an effective method to remove microplastics and nanoplastics from the human body. Here, we provide the first evidence that extracorporeal apheresis, a therapeutic technique established around the world, may have the potential to achieve this goal.

Microplastics (1 μm–5 mm) and nanoplastics (<1 μm) (MNPs) are small plastic particles originating from commercial production, such as cosmetics and medical drugs and from the degradation of large plastic waste. MNPs are virtually omnipresent and only lately the concerning magnitude and health dimension of this environmental threat is becoming evident (1, 2).

Due to current methodological limitations, we prefer to speak about MNPS or MNP-like structures, which may consist of MNPs combined with other molecules, such as proteins. It is crucial to emphasize that correct sampling and storage are extremely sensitive steps in the workflow, as contamination occurs instantly (2, 3). To ensure the reliability of findings, strict quality standards should always be applied. Given these limitations, recent studies reporting the presence of microplastics in numerous tissues, including the lung, heart, gut, liver, brain, and metabolically active tissues (4, 5), should be interpreted with some caution. Nonetheless, growing evidence suggest that MNPs may contribute to the development and progression of various conditions, including cardiovascular and metabolic diseases, infertility, cancer, and even neurodegenerative disorders such as dementia (5, 6). Moreover, it has been proposed that MNPs engulfed in adrenal tissue may alter steroidogenesis and cortisol levels (7, 8), and that perturbations in stress regulation may contribute to symptoms of chronic fatigue following viral infections. Additionally, MNPs may facilitate the transport of infectious particles into tissues and cellular compartments (9, 10), though further research is needed to confirm these mechanisms.

Given the ubiquitous presence of MNPs in the environment, completely avoiding exposure is unrealistic. While some initiatives promote a global strategy to reduce the intake of MNPs, there remains a critical need for an effective method to remove them from the human body. Therefore, our group recently suggested that extracorporeal therapeutic apheresis could be used to remove environmental factors (11). Apheresis is an extracorporeal technique used to selectively remove specific blood components, such as particular cells or plasma constituents (Figure 1A). Previously, we and others demonstrated that up to 70% of patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), including some with long COVID, reported a significant improvement in their symptoms following extracorporeal apheresis (12–15).

An astonishing rise in patients with ME/CFS has been linked to the increasing levels of environmental airborne particle matter 10 μm or less in diameter (16). In the current study, we have investigated whether therapeutic apheresis can remove MNP-like particles from

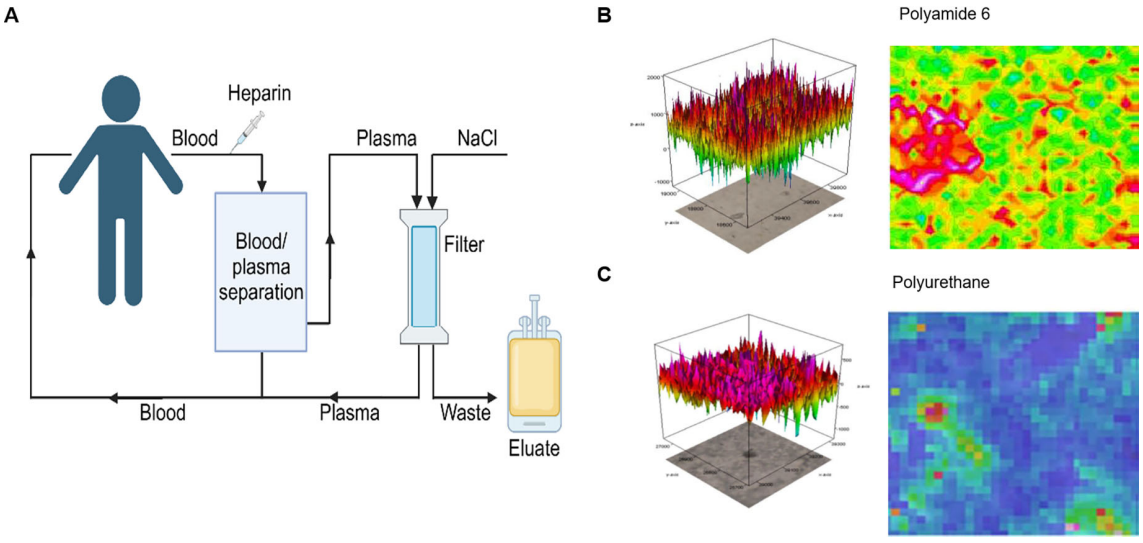

Figure 1. Extracorporeal therapeutic apheresis removes microplastic- and nanoplastic-like particles from human blood. (A) Schematics of an extracorporeal apheresis system. First blood is drawn from a large vein and processed through an apheresis machine. Then a porous membrane is used to separate blood cells from plasma. The plasma is processed through specific filters for removal of different blood components such as lipids or autoantibodies. After removal of the targeted component, the remaining blood components are reinfused into the patient through a second venous access. The components removed from the plasma, potentially including microplastics and nanoplastics, will be contained in the eluate. Created with BioRender.com. (B and C) Two examples from 21 patient samples demonstrating microplastics in the concentrated eluate removed from the patients' blood, measured by ATR-FT-IR. The full IR spectra, followed by analysis of individual spots, showed a 67.5% match with polyamide 6 (B) and a 35.3% match with polyurethane (PUR-WS) (C).

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the human body. Twenty-one patients with a confirmed diagnosis of ME/CFS related to a postinfectious syndrome, received at least two cycles of therapeutic apheresis with double filtration (INUSpheresis) (Figure 1A). The concentrated eluate sequestered from the blood circulation during apheresis was analyzed for MNP-like particles after each treatment using attenuated total reflection Fourier transform infrared (ATR-FT-IR) spectroscopy (for further details see *supporting online material*). The analysis of the patient eluates showed that 14 different substances or mixtures of substances could be detected only in the eluates from these patients with resemblance to for example polyamide 6 and a polyurethane, PUR-WS (Figure 1B and C). Polyamide 6, also known as nylon 6, is a synthetic polymer primarily produced as a fiber rather than a particle. For specialized applications, electrospun fibers are manufactured with diameters below 100 nm, which may explain why we can detect particles in eluates that were double filtered (blood separator and TKM58 apheresis filter) with pore sizes of $\leq$ 200 nm. Of note, this analysis does not quantitatively measure MNPs; it only determines whether MNP-like particles are present or not. The MNP-like particles found in eluates from patient samples were not present in any samples from the filter prerinse process (Supplementary Figure S1), indicating that they can only be attributed to the patient eluates. However, as ATR-FT-IR spectroscopy detects polyamide bonds, it should be noted that these could also originate partly from proteins.

As mentioned above, there is increasing evidence that MNPs can be associated with a number of health problems (5–8). However, the long-term effects and specific mechanisms still need to be further elucidated. Different analytical methods have been developed to identify and characterize MNPs, each with distinct capabilities and limitations in relation to morphology, chemical composition, and quantity (17). Until now, no methods have been reported for removing MNPs from the human body. In this study, we demonstrate for the first time that extracorporeal therapeutic apheresis might have this capability. However, larger patient cohorts and quantitative analyses, such as pyrolysis gas chromatography mass spectrometry, are required to confirm the effective removal of MNPs through therapeutic apheresis. This should include measuring MNP levels in plasma samples before and after apheresis, as well as in eluates, across multiple cycles. Such analyses will help determine particle removal from blood and tissues and assess correlations with symptom improvement in conditions like ME/CFS. We recommend a comprehensive study on the removal of MNPs using various filter systems with different pore sizes to develop strategies for both preventing uptake and facilitating detoxification of accumulated particles.

Ethics

All participants in the study have provided written consent.

Author Disclosures

G.P., R.S., and K.V.-B. work at INUS Medical Center AG in Cham, offering therapeutic apheresis as a treatment for conditions such as chronic fatigue.

Data Availability

The datasets generated during and/or analyzed during the current study are included in this published article (and its supplementary information files) or available from the corresponding author.

Author Contributions

RS and KVB designed research; GP, RS, and KVB collected the clinical data; TG, DK, AEA, and LP performed research. SRB, MY, WK, KVB, JL, and CS analyzed data. CS and SRB wrote the initial draft of the paper; All authors read and approved the manuscript.

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