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An *Ex Vivo* Study Examining Migration of Microplastics from an Infused Neonatal Parenteral Nutrition Circuit

Maaike Vercauteren,[1] Lucas Panneel,[3,4] Philippe G. Jorens,[4,5] Adrian Covaci,[5] Paulien Cleys,[5] Antonius Mulder,[3,4] Colin R. Janssen,[1,2] and Jana Asselman[1]

[1]Blue Growth Research Lab, Ghent University, Oostende, Belgium
[2]GhEnToxLab, Ghent University, Ghent, Belgium
[3]Neonatal Intensive Care Unit, Antwerp University Hospital, Edegem, Belgium
[4]Laboratory for Experimental Medicine and Paediatrics, University of Antwerp, Wilrijk, Belgium
[5]Toxicological Centre, University of Antwerp, Wilrijk, Belgium

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Introduction

The use of plastics in health care raises concerns about potential leaching of endocrine-disrupting plasticizers[1] and micro- and nanoplastics (MNPs). The leaching of particles from plastic health care equipment in the blood of intensive care patients has been associated with several health risks,[2] and as such, similar health risks could occur with leaching of microplastics.

To estimate the risk of MNPs administered via parenteral nutrition (PN) in premature neonates in the neonatal intensive care unit (NICU), more knowledge on the size, composition, and concentration of MNPs that can end up in the patients is needed.[3] Therefore, this pilot study aimed at estimating the migration of microplastics (MPs; >25 μm) from an infused PN circuit (both crystalloid and lipid) using an *ex vivo* experimental setup mimicking the clinical application as used in the NICU of the Antwerp University Hospital, Belgium.

Methods

An *ex vivo* experiment was set up to closely simulate the *in vivo* situation of neonatal PN administration, including both lipid emulsion (Neolipid) and crystalloid solution (Neobin), as described in Panneel et al.[4] ("Supporting data – Methods.docx"). We considered a premature neonate of 1 kg, postnatal day 0–5, with a mean daily fluid requirement of 120 mL/kg/d.[4] Samples were collected from each solution before infusion (T_0, collected with prerinsed steel needle) and after 12 (T_{12}), 24 (T_{24}), 48 (T_{48}), and 72 (T_{72}) hours of running through the infusion circuit. Experiments were repeated five times, with the last replicate only run for 48 h—collecting no sample at T_{72} due to practical problems. The samples were collected in prerinsed glass bottles covered with aluminum foil and stored [4°C, potassium hydroxide (KOH) added] until processing.

The ability of *in vivo*, in-line filters, standard practice during lipid administration, to prevent passage of MPs was tested in duplicate. Two filters (pore size: 1.2 μm) of different circuits of the lipid emulsion simulation were flushed with ultrapure water, both retro- and antegrade, and analyzed for MPs in the rinsing water.

MPs (>25 μm) were filtered (pore size: 10.0 μm, ø 25 mm; Omnipore Membrane filter; Merck) and analyzed using Fourier-transform infrared (FTIR) spectroscopy (Nicolet iN10 FTIR Spectrometer; ThermoFisher) for polymer identification, using methodology similar to that described before by Semmouri et al.[5] with the proper precautions such as cotton lab coats to avoid contamination.[5] Procedural blank samples (deionized water, $n = 4$) did not contain any microplastics. The MP concentrations were used to calculate the minimal and maximal administered dose for a 1 kg neonate in a clinical situation, based on the flow of the administered fluids (4.2 mL/h for crystalloid solution and 0.8 mL/h for lipid emulsion). Graphs were produced using the ggplot2 package (version 4.0.3) available in R Studio.

Results and Discussion

Microplastics in Parenteral Nutrition

The crystalloid solutions ($n = 24$) contained MPs with maximum concentrations found at T_0 and lowest at T_{72} (Figure 1). The most common polymer type was polyethylene terephthalate (PET, 71%, 49 particles), and 79% (53 particles) of MPs ranged between 25 and 175 μm, with the majority (41.8%) ranging between 75 and 125 μm (Figure 1). An interesting finding was that T_0 samples contained relatively more MPs of larger size (>200 μm) than samples at other time points. This finding could indicate that bigger MP particles could be present in the starting solution, either from contamination in the fluid or leaching from the infusion bag during storage.

The lipid emulsion ($n = 24$) contained 0.80 ± 0.65 MP/mL (excluding one of the T_{24} replicates showing a concentration of 10 MP/mL). These MP concentrations were higher compared to the crystalloid samples, which could indicate that a more lipophilic environment not only enhances the leaching of plasticizers[6] but also MPs. At T_0, the most dominant polymer type in the lipid emulsion was polypropylene (PP; 76%; 13 particles), the material of the syringe used in the circuit (Supporting data, "Supporting data – Analysis of the circuit.docx"). However, after infusion, PET was most dominant. In general, 80% (163 particles) of MPs had a length between 25 and 175 μm, with 32.5% between 25 and 75 μm (Figure 2).

In-Line Filtration

Antegrade and retrograde flushing resulted in 0.10 ± 0.14 MP/mL and 0.35 ± 0.21 MP/mL, respectively. On the filters, both PET (56%, 5 particles, mainly retrograde flushing) and PP (44%, 4 particles, mainly antegrade flushing) were found. Antegrade flushing showed MPs with smaller size (87.5 ± 59.7 μm) in comparison with retrograde flushing (150.9 ± 66.9 μm), although the number of MP (antegrade: 2 MPs; retrograde: 7 MPs) was quite low, making it impossible to draw any conclusions.

These results suggest that, as hypothesized, the in-line filter prevented a portion of MPs from entering neonates intravenously. However, the infused samples and the antegrade filtrates also suggested that still some MPs can end up in the

Address correspondence to Maaike Vercauteren. Email: Maaike.vercauteren@ugent.be

The authors declare that there are no conflicts of interests.

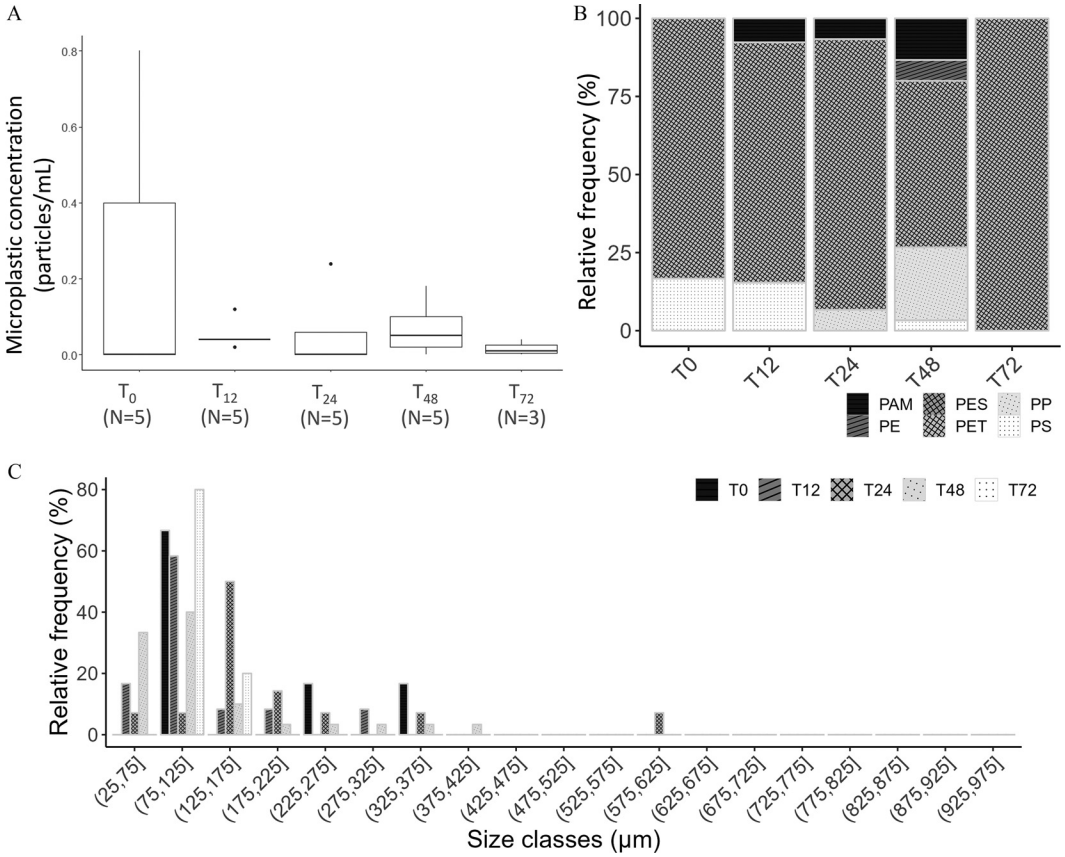

Figure 1. Overview of microplastic concentration (A), polymer composition (B), and size distribution (C) in the crystalloid solution collected in a simulated parenteral nutrition circuit and administered over a course of maximum 72 h with samples at time 0 (T0), T12, T24, T48, T72. The T0 measurements represent information on microplastics in the original fluid, without transition through the circuits. The number of samples per time point is indicated in panel A with "N=." Two particles (size 976 and 1,274.9 µm) are not included in the figure of the size distribution (Figure 1C). Plastic polymer types (Figure 1B), are polyacrylamide (PAM), polyester (PES), polypropylene (PP), polyethylene (PE), polyethylene terephthalate (PET), and polystyrene (PS). Corresponding numeric data of the figure can be found in Supplementary data at https://zenodo.org/records/10102884 ("Supporting data – Numeric data.docx").

patients—either via plastic sources distal to or by leaching through the filter. Previous studies showed up to 95% reduction of particle matter with the use of 0.2-µm filters in parenteral nutrition circuits,[7] therefore corroborating our results. An important conclusion is that the observed variability is inherent because the release of MPs is assumed to be dependent on many factors, such as connections, positioning and handling of tubing, filters, storage conditions, etc. Moreover, only a limited number of samples was analyzed in this study, so more data are necessary.

Microplastic Exposure Assessment

Despite the presence of an in-line filter (0.2 µm), based on our data 1 to 52 MP particles (>25 µm) could be administered over a course of 72 h via the crystalloid solution to a neonate of 1 kg. Nonetheless, if the solution would not be filtered—considering extrapolation from the maximum T_0 MP concentration (0.80 MP/mL at a flow of 4.2 mL/h for 72 h)—the maximum number of MP particles could be around 241 MP particles. During lipid administration, based on our data, exposure is estimated to be 8–115 MP particles in a 1-kg neonate over 72 h, despite the presence of a 1.2-µm in-line filter.

The MP size ranges found in PN in this study exceeded the diameter of lung and tissue capillaries.[8] Therefore, these MPs may cause obstruction and subsequent granulomatous microvascular and pulmonary inflammation as already demonstrated by other types of particles.[9] However, the direct health effects of MPs are currently unknown.[10] It is important to note that, because of analytical size limitations, no information is available on particles <25 µm, which could cross cellular barriers and cause systemic effects.[11]

In conclusion, our data indicated, for the first time, that exposure to MPs (>25 µm) leaching from intravenous lines might be an additional and direct exposure route in humans and in neonates in particular. Nonetheless, to understand the importance of this exposure route, increased MP concentration measurements are needed to decrease variability in the observations. In-line filters seem capable of reducing the number of microplastics entering the patients intravenously, although no absolute filtration was observed.

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Detailed description of the methods and raw data can be found via doi 10.5281/zenodo.10102884.

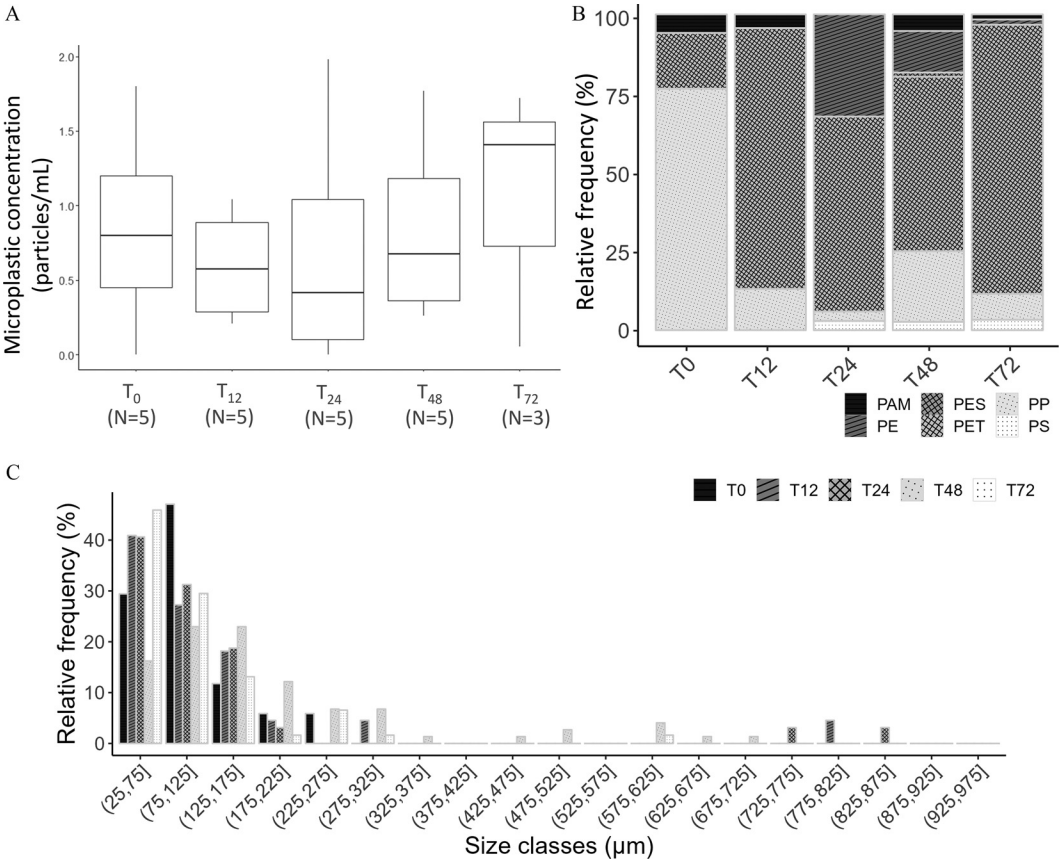

Figure 2. Overview of microplastic concentration (A), polymer composition (B), and size distribution (C) in the lipid emulsion collected in a simulated parenteral nutrition circuit and administered over a course of maximum 72 h with samples at time 0 (T0), T12, T24, T48, T72. The T0 measurements represent information on microplastics in the original fluid, without transition through the circuits. The number of samples per time point is indicated in panel A with "N=." Plastic polymer types (Figure 2B) are polyacrylamide (PAM), polyester (PES), polypropylene (PP), polyethylene (PE), polyethylene terephthalate (PET), and polystyrene (PS). Corresponding numeric data of the figure can be found in Supplementary data at https://zenodo.org/records/10102884 ("Supporting data – Numeric data.docx").

References

1. Malarvannan G, Onghena M, Verstraete S, van Puffelen E, Jacobs A, Vanhorebeek I, et al. 2019. Phthalate and alternative plasticizers in indwelling medical devices in pediatric intensive care units. J Hazard Mater 363:64–72, PMID: 30308366, https://doi.org/10.1016/j.jhazmat.2018.09.087.
2. Foster JP, Richards R, Showell MG, Jones LJ. 2015. Intravenous in-line filters for preventing morbidity and mortality in neonates. Cochrane Database Syst Rev 2015(8):CD005248, PMID: 26244380, https://doi.org/10.1002/14651858.CD005248.pub3.
3. Gopinath PM, Parvathi VD, Yoghalakshmi N, Kumar SM, Athulya PA, Mukherjee A, et al. 2022. Plastic particles in medicine: a systematic review of exposure and effects to human health. Chemosphere 303(pt 3):135227, PMID: 35671817, https://doi.org/10.1016/j.chemosphere.2022.135227.
4. Panneel L, Cleys P, Breugelmans C, Christia C, Malarvannan G, Poma G, et al. 2023. Neonatal exposure to phthalate and alternative plasticizers via parenteral nutrition. Int J Pharm 631:122472, PMID: 36526146, https://doi.org/10.1016/j.ijpharm.2022.122472.
5. Semmouri I, Vercauteren M, Van Acker E, Pequeur E, Asselman J, Janssen C. 2023. Distribution of microplastics in freshwater systems in an urbanized region: a case study in Flanders (Belgium). Sci Total Environ 872:162192, PMID: 36781133, https://doi.org/10.1016/j.scitotenv.2023.162192.
6. Bagel S, Dessaigne B, Bourdeaux D, Boyer A, Bouteloup C, Bazin J-E, et al. 2011. Influence of lipid type on bis (2-ethylhexyl)phthalate (DEHP) leaching from infusion line sets in parenteral nutrition. JPEN J Parenter Enteral Nutr 35(6):770–775, PMID: 21868720, https://doi.org/10.1177/0148607111414021.
7. Ayres JD, Mahler HC. 2021. Assessing the utility of in-line intravenous infusion filters. J Pharm Sci 110(10):3325–3330, PMID: 34139262, https://doi.org/10.1016/j.xphs.2021.06.022.
8. Levick JR. 2013. *An Introduction to Cardiovascular Physiology*. Oxford, UK: Butterworth-Heinemann.
9. Puntis JW, Wilkins KM, Ball PA, Rushton DI, Booth IW. 1992. Hazards of parenteral treatment: do particles count? Arch Dis Child 67(12):1475–1477, PMID: 1489228, https://doi.org/10.1136/adc.67.12.1475.
10. SAPEA (Science Advice for Policy by European Academies). 2019. A scientific perspective on microplastics in nature and society. Berlin, Germany: SAPEA. https://doi.org/10.26356/microplastics [accessed 10 November 2020].
11. Lee Y, Cho S, Park K, Kim T, Kim J, Ryu D-Y, et al. 2023. Potential lifetime effects caused by cellular uptake of nanoplastics: a review. Environ Pollut 329:121668, PMID: 37087090, https://doi.org/10.1016/j.envpol.2023.121668.