

Title of the project:	
Comparison of pre- and post-dilution hemodiafiltration modalities – effects on biocompatibility and solute clearance in children	
Principal investigator	Year of award
Professor Rukshana Shroff	2021
Please provide an overall summary of the project (max 500 words)	
Project Summary: A Randomised Cross-over Trial of Pre- vs Post-Filter Haemodiafiltration in Children on Maintenance Dialysis This multicentre, randomised cross-over trial — funded by an ESPN (European Society of Paediatric Nephrology) research grant — was designed to compare two haemodiafiltration (HDF) modalities in children with end-stage kidney disease: pre-filter HDF (pre-HDF) and post-filter HDF (post-HDF). Background & Rationale While post-HDF has been shown to improve cardiovascular outcomes and growth in children compared to conventional haemodialysis, pre-HDF can deliver substantially higher convection volumes. However, evidence comparing the two HDF modalities in children was absent. The study aimed to fill this gap by rigorously comparing their effects on solute removal, inflammation, nutrition, and blood pressure. Study Design The trial was conducted across four paediatric dialysis centres in Türkiye, the UK, France, and Germany (February 2021 – November 2022). After a 4-week wash-out period in post-HDF, 21 children (median age 15.1 years; 71% female) were randomised to either pre-HDF or post-HDF for 4 weeks each, then crossed over. All other dialysis parameters (machine, dialyser, blood/dialysate flow rates, session duration) were kept strictly constant across both arms. The primary outcome was the reduction in α1-microglobulin (α1M), a large middle-molecular weight uraemic retention solute. Key Findings • Convection volumes were more than twice as high in pre-HDF (36.2 L/m² BSA/session) versus post-HDF (14.3 L/m² BSA/session). • Middle-MW solute removal: Pre-dialysis levels of α1M [104 (92;117) vs 122 (111;130) ng/ml, p=0.009] , β2-microglobulin [17.7 (15.1;20.6) vs 23.2 (19.8;27.0) mg/l, p=0.003] were significantly lower with pre-HDF, and reduction ratios for α1M [%26.4 (11.3;42.9) vs 13.1 (0.48;24.0), p=0.004] and β2M [%77.2 (73.3;82.7) vs 72.6 (65.7;78.3), p=0.006] were higher — demonstrating superior clearance of middle and large middle-MW toxins. • Protein-bound uraemic toxins: Reduction ratios for total indoxyl sulfate (p=0.04) and p-cresyl sulfate (p=0.02) were significantly higher with pre-HDF, though other protein-bound toxins did not differ significantly between modalities. • Small-MW solutes: Kt/V and creatinine/phosphate clearances were comparable between modalities, and — importantly — serum albumin levels were preserved in pre-HDF, contrasting with prior reports of albumin loss. • Inflammation: Pre-dialysis hsCRP (p=0.02), TNFα(p<0.001), and IL-10 (p=0.03) concentrations were significantly lower with pre-HDF, indicating a more favourable inflammatory profile.	

- **Blood pressure:** Diastolic BP was significantly higher in pre-HDF (diastolic BP-SDS: 1.40 (0.70–2.10) vs 0.46 (–0.15–1.21), $p=0.01$), associated with higher replacement volumes and greater sodium exposure — a clinically important finding, particularly in patients receiving the highest convection volumes.
- **Nutritional markers and patient-reported outcomes** did not differ meaningfully between the two modalities.

Conclusions

Pre-HDF achieves superior removal of middle and large middle-MW uraemic toxins and is associated with a better inflammatory milieu, without compromising small-MW clearance or albumin levels. However, a subset of patients may experience higher blood pressure, likely due to increased sodium load from larger replacement volumes.

How was the grant used for the project? (max 200 words)

We applied the ESPN grant to provide the fee of couriering samples from study centers to central laboratory at GOSH, London and for the costs of the following measurements : Cystatin-C, IL-6, TNF-alpha, Leptin, Ghrelin, Cholecystokinin, Hepcidin, ADMA, SDMA and p-cresyl sulphate and Indoxyl sulfate, Indole acetate, Hippuric acid.

Please list all publications completed, with links to open access publications where available

No peer-reviewed publications have been completed to date. The study manuscript is currently under major revision at *Kidney International*. No open access links are available at this stage.

Are any other publications planned?

The primary manuscript reporting the main findings of this randomised cross-over trial is currently under review at *Kidney International* and is undergoing major revision. Publication is anticipated following the completion of this revision process. No additional publications are planned at this time.

Please list all presentations relating to the project

- **55th European Society of Paediatric Nephrology (ESPN) Annual Congress, Vilnius Lithuania:** Presentation of abstract as a 3-minute oral pitch.
- **20th International Pediatric Nephrology Association (IPNA) Congress, Cape town, South Africa:** Presentation of abstract as a 3-minute oral pitch. The abstract was selected as one of the **Best Abstracts** at this meeting.