

DIALYSIS. EXTRACORPOREAL DIALYSIS: TECHNIQUES AND ADEQUACY

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URAEMIC TOXIN CONCENTRATION VARIABILITY IN HD PATIENTS: CAN WE STILL RELY ON THE RESULTS OF CROSS-SECTIONAL STUDIES?

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Introduction and Aims: Numerous cross-sectional studies evaluated in haemodialysis patients the association of specific uraemic toxin concentrations on patient outcomes at a given time point. It has however not been investigated whether in stable patients, the pre-dialysis concentration of uraemic toxins remains constant. We therefore quantified the variability of uraemic toxin concentrations in haemodialysis patients over a period of 16 weeks.

Methods: This prospective study included 18 stable chronic haemodialysis patients: 3 women, 11 diabetics, 12 with well functioning arteriovenous fistula, 5 with double lumen central venous catheter, and 1 with a PTFE graft combined with a single lumen central venous catheter. Patients were 72.5±10.1 years old, spent 55.7±30.1 months on dialysis, and had a residual renal function of 3.5±3.0mL/min. Blood samples were collected at the midweek session of week 0, 1, 2, 3, 4, 8, 12, and 16. During the study

period, the dialyser type (all high flux) and dialysis mode (17 patients on post dilution haemodiafiltration and 1 on haemodialysis) were maintained. During the test sessions, blood and dialysate flows were 311±21 and 530±39mL/min, respectively, while ultrafiltration was set according to the need of the patient. Kt/Vurea was monthly assessed according to the single-pool Daugirdas formula. Blood samples were collected predialysis and were immediately centrifuged after which plasma was stored at -80°C until batch analysis. Samples were analysed for urea, creatinine (Crea), phosphorus (P), and uric acid (UA), and for total and free concentrations of protein-bound solutes p-cresylglucuronide (PCG), hippuric acid (HA), indole acetic acid (IAA), indoxyl sulfate (IS), p-cresylsulfate (PCS), and 3-carboxy-4-methyl-5-propyl-2-furanpropionic acid (CMPF). The coefficient of variation (%CV) to describe inter- and intra-patient variability was calculated as the ratio of the standard deviation (i.e. square root of the variance component) to the mean. Differences between the inter- and intra-patient % CV was checked with the paired t-test.

Results: Overall Kt/V was 1.6±0.3 with %CV of only 13% (intra-patient) and 12% (inter-patient), and no trend in time. The intra-patient %CV is in the range 7-14% for concentration of the small water soluble solutes urea, Crea, P, and UA, while %CV is in the range 19%-25% for total concentrations of highly bound solutes IS, PCS, and CMPF, and even 36-46% for total concentrations of less bound solutes PCG, HA, and IAA, and for free concentrations of all studied protein-bound solutes. The inter-patient %CV, being in the range 16-27% for concentrations of small water soluble solutes, and 42-119% for the total and free fractions of the protein-bound solutes, is however significantly larger as compared to the intra-patient %CV (p<0.001).

Conclusions: Uraemic toxin concentrations vary largely among stable haemodialysis patients, but also intra-patient variability is non-negligible, especially for the protein-bound solutes. It is unclear how this intra-patient variability effects on the interpretation of the association between concentrations of uraemic toxins and outcomes.