Kinetic modeling as guide for dialysis prescription in acute neonatal hyperammonaemia:
an example using CarpeDiem and Fresenius 4008 machine

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Background
Acute neonatal hyperammonaemia is associated with poor neurological outcomes and high mortality. As these outcomes are inversely related to the duration of the hyperammonaemic coma, prompt management that guarantees a fast decline in serum ammonia is crucial. Using our experience with different dialysis machines, we developed a kinetic model for acute neonatal hyperammonaemia to draft a dialysis prescription protocol that can ensure a fast decline in serum ammonia (goal:<400µmol/L in <4hours).

Methods
From all dialysis sessions performed in 2020 in our centre in newborns with hyperammonaemia, dialyzer clearance and extraction ratio were calculated using intradialytic ammonia concentration-time curves. A single compartment kinetic model with a distribution volume of 60%-80% of body weight was assumed, and generation was derived from the interdialytic concentration increase.. The calibrated single compartmental model was further used to simulate serum ammonia decline in infants of 2-5kg for different ammonia start concentrations (3000, 1500, 800, 400, 200µmol/L), dialysis machines/dialyzers and settings (blood flow Q_B 30-50mL/min).

Results
Four patients (3.24±0.40 kg) underwent 13 dialyses: 5 with the 4008 machine and FXPaed dialyzer (Fresenius Medical Care, Germany); and 8 with the CarpeDiem machine (50% with 0.15m² respectively 0.25m² dialyzer) (Medtronic, USA). Q_B was 30-35mL/min (4008-FXPaed), 22-35mL/min (CarpeDiem 0.15), and 30-34mL/min (CarpeDiem 0.25). Extraction ratios were 38±5% for 4008-FXPaed, 10±3% and 13±3% in the CarpeDiem 0.15m² and 0.25m² dialyzer. Generation was 0.40±0.25µmol/min, with no observed impact on dialyzer clearance and extraction ratio. For start concentrations of 3000µmol/L (3kg), the time to drop <400µmol/L was, with 4008-FXPaed, 315 and 190min for a Q_B of 30 and 50mL/min, respectively, while it was 205 and 125min for a start concentration of 1500µmol/L, and 110 and 65min for a start concentration of 800µmol/L. In general, for start concentrations >800µmol/L in 3kg child, the CarpeDiem machine was found inadequate to decrease serum ammonia in <4h. Increasing body weight (5kg) resulted in longer time intervals to reach target.

Conclusion
Kinetic models can guide our management decisions and treatment protocols by predicting which treatment goals can be reached with a particular dialysis prescription, available resources and/or dialysis modality.