A276 - The effect on ketogenesis of withholding early parenteral nutrition in critically ill children, as a potential mediator of the improved intensive care outcomes

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Introduction:
In adults and children, accepting a macronutrient deficit early during critical illness by withholding parenteral nutrition (PN) for 1 week (late PN) accelerates weaning from mechanical ventilation, reduces infections and shortens ICU stay as compared with early supplementing insufficient enteral nutrition with PN (early PN). We hypothesized that these outcome benefits are in part mediated by fasting-induced ketogenesis.

Methods:
This is a secondary analysis of the PEPaNIC RCT. First, to identify a potential time point of maximal effect of late vs. early PN, we quantified plasma 3-hydroxybutyrate (3HB) in a matched subset of 96 patients with a PICU stay of ≥5 days. Thereafter, we quantified plasma 3HB and insulin on that “maximal effect” day (or last day for shorter stayers; 1142 patients with available sample). Associations of 3HB with outcomes were assessed with multivariable logistic regression and Cox proportional hazard analyses, adjusted for baseline risk factors and randomization. In sensitivity analyses, models were further adjusted for key regulators of ketogenesis to assess whether any effect was direct or indirect.

Results:
Late PN increased plasma 3HB as compared with early PN, with maximal effect on day 2 (P<0.0001 for day 1 to 5 and for the “maximal effect” day in the 1142 patients). Adjusted for baseline risk and randomization, plasma 3HB associated with a higher likelihood of earlier live weaning from mechanical ventilation (P=0.0002) and of earlier live PICU discharge (P=0.004). As plasma 3HB replaced the effect of the randomization, the 3HB effect statistically explained these benefits of the randomization. Further adjustment for key regulators of ketogenesis did not alter these findings. Plasma 3HB did not independently associate with the risk of infections and mortality.

Conclusion:
Withholding early PN increased ketogenesis in critically ill children, an effect that statistically mediated part of its clinical benefits.