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Reconciling Nutrition Support Supplementation with the Deeper Metabolic Picture of Muscle Wasting in Dialysis Patients - Understanding the Science of Nutrition Intervention

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Background: Protein Energy Wasting (PEW) in maintenance hemodialysis (HD) patients is marked by suboptimal dietary protein and dietary energy intakes. Muscle proteolysis is enhanced in PEW, driven by metabolic acidosis, uremia, insulin resistance and inflammation. To correct PEW, oral nutritional supplementation (ONS) is recommended by the International Society of Renal Nutrition and Metabolism (ISRNM) as a first therapeutic choice whilst Intradialytic parenteral nutrition (IDPN) enters the picture for patients having poor oral/ enteral tolerance. Method: Recruitment for the HemoDialysis Nutrition Study's planned nutritional interventions required HD patients with PEW identified through ISRNM criteria (any 3 of 4) in a multicentre open-label randomized controlled trial. Patients randomized to ONS (n=29) received a renal-specific commercial product and nutritional counselling (NC) for 6 months, whilst the control group (n=27) received NC only. Patients randomized to IDPN intervention (n=23) received a commercial standard 3-chamber bag along with NC for 6 months whilst the control group (n=21) received NC only. Treatment effects were evaluated as per body weight, skinfolds, biochemistry, malnutrition-inflammation-score, quadriceps muscle status assessed using ultrasound imaging (US), handgrip strength (HGS) method, body composition, appetite and QoL. Metabolite profiling of fasting pre-dialysed plasma (baseline, 3 and 6 months) was performed using 1-H nuclear magnetic resonance spectroscopy at 600 MHz. Results: Metabolites separately unique to ONS and IDPN feeding elicited significant group X time interactions in comparison to patients just receiving nutrition counseling. The emergence of these different metabolites via the respective feeding routes also implied they were mediated through different metabolic pathway involvement. Irrespective of feeding routes, either supplementation correlated to improvements in quadriceps muscle status as well as mitigating PEW. Conclusion: Both ONS and IDPN

treatments compared to only nutrition counseling elicited favorable metabolic pathway modulation in PEW patients on HD clearly dependent on the nature and route of feeding products.

Keywords: PEW, Muscle wasting, ONS, IDPN, Metabolomics