Research Week 2020

Large Neutral Amino Acid Supplementation Improves Clinical Efficacy of Usual Care in Adult PKU

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Abstract

Introduction

PKU requires lifelong management, but the childhood PKU diet does not accommodate for post-adolescent patient variations, including: (1) the diet's effect on blood phenylalanine (Phe) concentrations, and (2) the therapeutic benefits of prescribed blood Phe targets. Most adult patients discontinue the inflexible diet, and are exposed to PKU's adverse effects. Research supports large neutral amino acids (LNAAs) as potential alternative strategy; we propose an additive LNAA strategy.

Objective

We aim to evaluate the clinical efficacy of a combined treatment strategy: usual care (the PKU diet) with LNAA supplementation.

Methods

An N-of-1 RCT was used to compare control and combined treatments: usual care (A) and usual care +LNAAs (B). A priori design randomly alternated 3 pairs of ~8-week treatment periods (ABBAAB). The adult subject historically experienced persistent symptoms, despite achieving prescribed blood Phe control (above U.S. target but within European guidelines). A run-in period established baseline measures and LNAA dose responsiveness (0.22g/kg PheBLOC™). Neuropsychological and biological treatment responses were assessed using the PKU-QoL Questionnaire, blood Phe, and Phe:Tyr ratio. Treatment comparisons utilized mean values across repeating periods.

Results

PKU-QoL scores supported clinical superiority for usual care +LNAAs, as (1) symptom frequencies fell to zero and (2) negative dietary impact scores decreased. Blood analysis showed marked Phe:Tyr decrease (A=14.1; B=3.1), but no significant change in Phe levels

(B= -14.9%). Due to symptom resurgence following the withdrawal of usual care +LNAAs, we made an ethical decision to end the experiment after two cycles (ABBA).

Conclusions

In this single-subject investigation, usual care +LNAAs corresponded with improved symptoms, without blood Phe changes. Moreover, the PKU biomarker Phe:Tyr significantly responded to the combined treatment and better correlated with symptom changes. These findings suggest clinical efficacy, and repeated investigation, with additional subjects, is needed to establish the potential benefits of additive LNAA strategies for adult PKU management.