The Indicator Amino Acid Oxidation Method with the Use of L-[1-13C]Leucine Suggests a Higher than Currently Recommended Protein Requirement in Children with Phenylketonuria.


Abstract

BACKGROUND: Phenylketonuria is characterized by mutations in the Phe hydroxylase gene that leads to the accumulation of Phe in plasma and the brain. The standard of care for phenylketonuria is nutritional management with dietary restriction of Phe and the provision of sufficient protein and energy for growth and health maintenance. The protein requirement in children with phenylketonuria is empirically determined based upon phenylketonuria nutritional guidelines that are adjusted individually in response to biochemical markers and growth.

OBJECTIVE: We determined dietary protein requirements in children with phenylketonuria with the use of the indicator amino acid oxidation (IAAO) technique, with L-[1-13C]Leu as the indicator amino acid.

METHODS: Four children (2 males; 2 females) aged 9-18 y with phenylketonuria [mild hyperphenylalanemia (mHPA); 6-10 mg/dL (360-600 μmol/L)] were recruited to participate in ≥7 separate test protein intakes (range: 0.2-3.2 g ⋅ kg⁻¹ ⋅ d⁻¹) with the IAAO protocol with the use of L-[1-13C]Leu followed by the collection of breath and urine samples over 8 h. The diets were isocaloric and provided energy at 1.7 times the resting energy expenditure. Protein was provided as a crystalline amino acid mixture based on an egg protein pattern, except Phe and Leu, which were maintained at a constant across intakes. Protein requirement was determined with the use of a 2-phase linear-regression crossover analysis of the rate of L-[1-13C]Leu tracer oxidation.

RESULTS: The mean protein requirement was determined to be 1.85 g ⋅ kg⁻¹ ⋅ d⁻¹ (R² = 0.66; 95% CI: 1.37, 2.33). This result is substantially higher than the 2014 phenylketonuria recommendations (1.14-1.33 g ⋅ kg⁻¹ ⋅ d⁻¹; based on 120-140% above the current RDA for age).

CONCLUSIONS: To our knowledge, this is the first study to directly define a quantitative requirement for protein intake in children with mHPA and indicates that current protein

recommendations in children with phenylketonuria may be insufficient. This trial was registered at clinicaltrials.gov as NCT01965691.

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**KEYWORDS:** IAAO; phenylalanine hydroxylase; phenylketonuria; protein requirements; stable isotopes

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