

Research update in PKU

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MDDA retreat, Sydney, September 2016

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Low protein diets in PKU: goals of therapy

- Good metabolic control
“Avoid too much phenylalanine”
- Normal growth and development
“Provide sufficient protein for growth”

Practices differ around the world

- Treatment recommendations are based on:
 - theoretical considerations
 - personal experience
 - small or large cohort retrospective studies
 - rarely, on double-blind, placebo-controlled studies
- “Local” practices may change based on availability of foods, cultural habits and diets etc.
- There is a trend towards harmonisation of treatment practices around blocks of countries



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European guidelines on diagnosis and treatment of PKU

Van Spronsen F J ¹, Van Wegberg A M J ¹, Ahring K ², Belanger-Quintana A ³, Blau N ^{4 5}, Bosch A M ⁶, Burlina A ⁷, Campistol J ⁸, Feillet F ⁹, Gizewska M ¹⁰, Huijbregts S C J ¹¹, Kearney S ¹², Leuzzi V ¹³, Maillot F ¹⁵, Muntau A C ¹⁶, Trefz F ⁴, Van Rijn M ¹, Walter J H ¹⁷, MacDonald A ¹⁴



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Vulnerability and resilience to phenylalanine in PKU patients

Manti F¹, Nardecchia F¹, Paci S⁴, Chiarotti F³, Carducci C², Dalmazzone S⁴, Giordano L⁴, Cefalo G⁴, Banderali G⁴, Leuzzi V¹

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Social-cognitive functioning and social skills in patients with early treated phenylketonuria: a PKU-COBESO study

Rianne Jahja¹ • Francjan J. van Spronsen¹ • Leo M. J. de Sonnevile² • Jaap J. van der Meere³ • Annet M. Bosch⁴ • Carla E. M. Hollak⁴ • M. Estela Rubio-Gozalbo⁵ • Martijn C. G. J. Brouwers⁵ • Floris C. Hofstede⁶ • Maaïke C. de Vries⁷ • Mirian C. H. Janssen⁷ • Ans T. van der Ploeg⁸ • Janneke G. Langendonk⁸ • Stephan C. J. Huijbregts²

Results PKU-patients showed poorer social-cognitive functioning and reportedly had poorer social skills than controls (regardless of general cognitive abilities). Quality of social-cognitive functioning was negatively related to recent Phe-levels and Phe-levels between 8 and 12 years for adolescents with PKU. Quality of social skills was negatively related to lifetime phenylalanine levels in adult patients, and specifically to Phe-levels between 0 and 7, and between 8 and 12 years. There were no differences with respect to social outcome measures between the BH₄ and non-BH₄ groups.

Conclusion PKU-patients have Phe-related difficulties with social-cognitive functioning and social skills. Problems seem to be more evident among adolescents and adults with PKU. High Phe-levels during childhood and early adolescence seem to be of greater influence than current and recent Phe-levels for these patients.



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Behaviour and quality of life in tyrosinemia type 1 patients compared to phenylketonuria patients and healthy controls

Van Vliet K¹, Van Ginkel W G¹, Jahja R¹, Daly A², MacDonald A², De Laet C³, Cassiman D⁴, Eyskens F⁵, Korver-Keularts I⁶, Goyens P J³, McKiernan P J², Huijbregts S C J⁷, Van Spronsen F J¹

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Pharmacological chaperones as an alternative treatment for phenylketonuria

Aubi O¹, Underhaug J¹, Ying M¹, Knappskog P M³, Hjelmdal E¹, Allegri G², Thony B², Martinez A¹

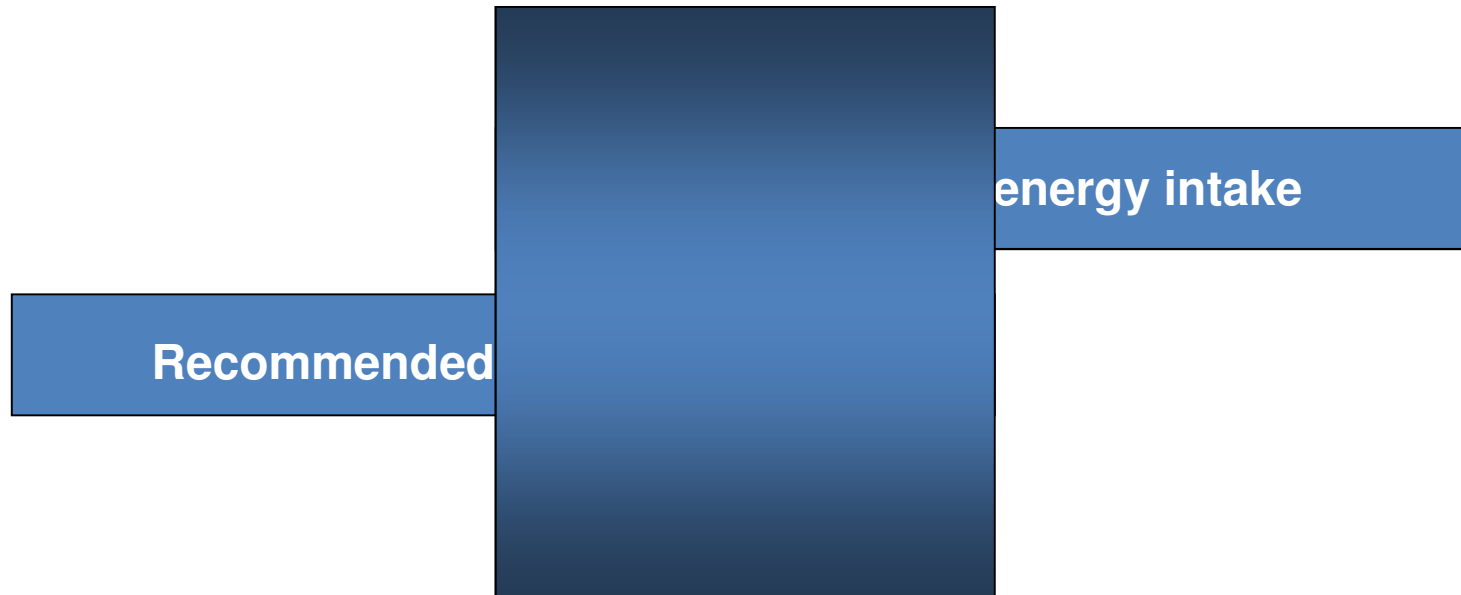
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The relationship between protein and energy intake
and nutritional outcome in Inborn Errors of Metabolism

Background

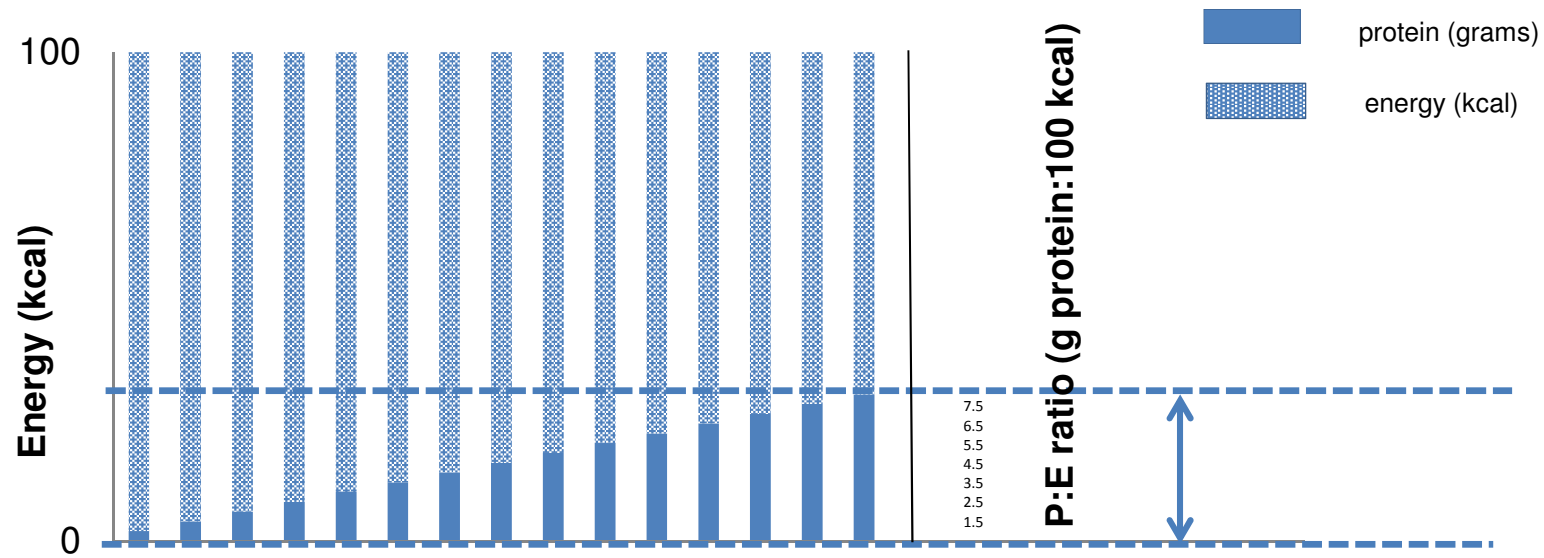
- Protein requirements are based on:
 - Adequate energy intake in order to
 - Utilise protein efficiently
 - Maintain Nitrogen balance
 - Allows tissue synthesis & growth
 - Protein of high & low biological value sources for
 - digestibility
 - amino acid content & ratios

Is it possible or beneficial to combine protein and energy recommendations into a single index?



Protein to Energy (P:E) Ratio

What is a safe P:E ratio (g protein: 100kcal)?



Aims

- To consider the inter-dependence of protein & energy given the severity of dietary restrictions & that estimates of requirements are made separately
- A single index to define adequacy?
The protein to energy ratio

Questions

- What is the growth pattern of patients with P-IEM?
- Do our patients get enough protein?
- Do our patients get enough energy?
- What is the protein to energy ratio of our patients' diets?
- What are the relationships between dietary intake and growth and body composition ?

Patients groups

Approach	Subjects to date	
Retrospective case history analysis using longitudinal data: <ul style="list-style-type: none"> • Growth • Dietary intake DOB: 1976 – 2014	PKU	70
	Tyrosinaemia	15
	Maple Syrup Urine disease	15
	Urea Cycle Disorder	43
	Organic acidaemia	28
	ATP production disorders	34
	Long chain Fatty acid oxidation disorders	20
	Glycogen storage disorder	23
	Total	248
	Prospective Longitudinal <ul style="list-style-type: none"> • Growth • Dietary intake • Body composition • Nutritional bloods DOB: 1995 - 2014	PKU
Tyrosinaemia		4
Maple Syrup Urine disease		4
Urea Cycle Disorder		7
Organic acidaemia		13
ATP production disorders		6
Long chain Fatty acid oxidation disorders		10
Glycogen storage disorder		10
Total		91

Method

- Document nutritional outcomes
 - Growth
 - Body composition
- Document dietary intake
 - Protein
 - Energy
 - P:E ratio
 - Confirm adequacy
- Examine associations between dietary intake and nutritional outcomes
 - Determine a 'safe' P:E ratio as a practical clinical tool

Can we estimate a 'safe' P:E ratio?

**1.5 - ~3 g
protein/100kcal?**

- A ratio > 1.5 g protein/100kcal is associated with improved weight and height z score without increasing BMI z-score
- A ratio > 3 g protein/100kcal may be associated with higher weight z score with no benefit in fat mass percentage.

Clinical messages

- As some children with OA and UCD have low weight & height z-scores, caution must be taken with increasing weight z-score as this may result in overweight.
- Providing more protein than required may not improve linear growth
- High energy intakes >180% BMR may not improve growth
- Providing natural protein to tolerance may improve body composition

Thank you

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