Research update in protein-IEM

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Low protein diets in IEM: goals of therapy

- Good metabolic control

  “Avoid too much protein”

- Normal growth and development

  “*Provide sufficient protein for growth”*

- During times of illness there is (a risk of) catabolism

  “Avoid / Reverse catabolism: provide sufficient calories”

  “Assume catabolism: stop protein intake”

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

Van Vliet K [1], Van Ginkel W G [1], Jahja R [1], Daly A [2], MacDonald A [2], De Laet C [3], Cassiman D [4], Eyskens F [5], Korver-Keularts I [6], Goyens P J [3], McKiernan P J [2], Huijbregts S C J [7], Van Spronsen F J [1]

[1]Div Metab Dis, Bea Child Hosp, UMCG, Groningen, Netherlands, [2]Birmingham Child Hosp, Birmingham, United Kingdom, [3]Univ Child Hosp Queen Fabiola, Brussels, Belgium, [4]Univ Hosp Gasthuisberg, Leuven, Belgium, [5]Queen Paola Child Hosp, Antwerp, Belgium, [6]Maastricht Univ Med Center, Maastricht, Netherlands, [7]Univ Leiden, Leiden, Netherlands

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Pharmacological chaperones as an alternative treatment for phenylketonuria

Aubi O [1], Underhaug J [1], Ying M [1], Knappskog P M [3], Hjelmdal E [1], Allegri G [2], Thony B [2], Martinez A [1]

[1]Dept Biomedicine, Univ Bergen, Bergen, Norway, [2]Dept Metab Dis, Univ Child Hosp, Zurich, Switzerland, [3]C Med Gen-Mol Med, Haukeland Univ Hosp, Bergen, Norway

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A potential novel treatment for CPS1 deficiency based on pharmacological chaperones

Diez-Fernandez C [1], Spodenkiewicz M [1], Underhaug J [2], Martinez A [2], Haeberle J [1]

[1]Univ Child Hosp, Div Metab, Zurich, Switzerland, [2]Univ Bergen, Biorecogn Dept, Bergen, Norway

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Functional characterization of missense mutations identified in methylmalonic aciduria *cblB* type and rescue by pharmacological chaperone therapy

Brasil S [1 2 3], Briso-Montiano A [1 2 3], Underhaug J [6], Merinero B [1 3 4 5], Desviat R L [1 2 3 4], Ugarte M [1 3 4], Martinez A [6], Perez B [1 2 3 4 5]

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Linear growth is reduced in patients with urea cycle disorders

Assatourian L [1], Trinh M [2], Macleod E [1], Simpson K [1], Park D [2], Ah Mew N [1], Members of the Urea Cycle Disorders Consortium[3]

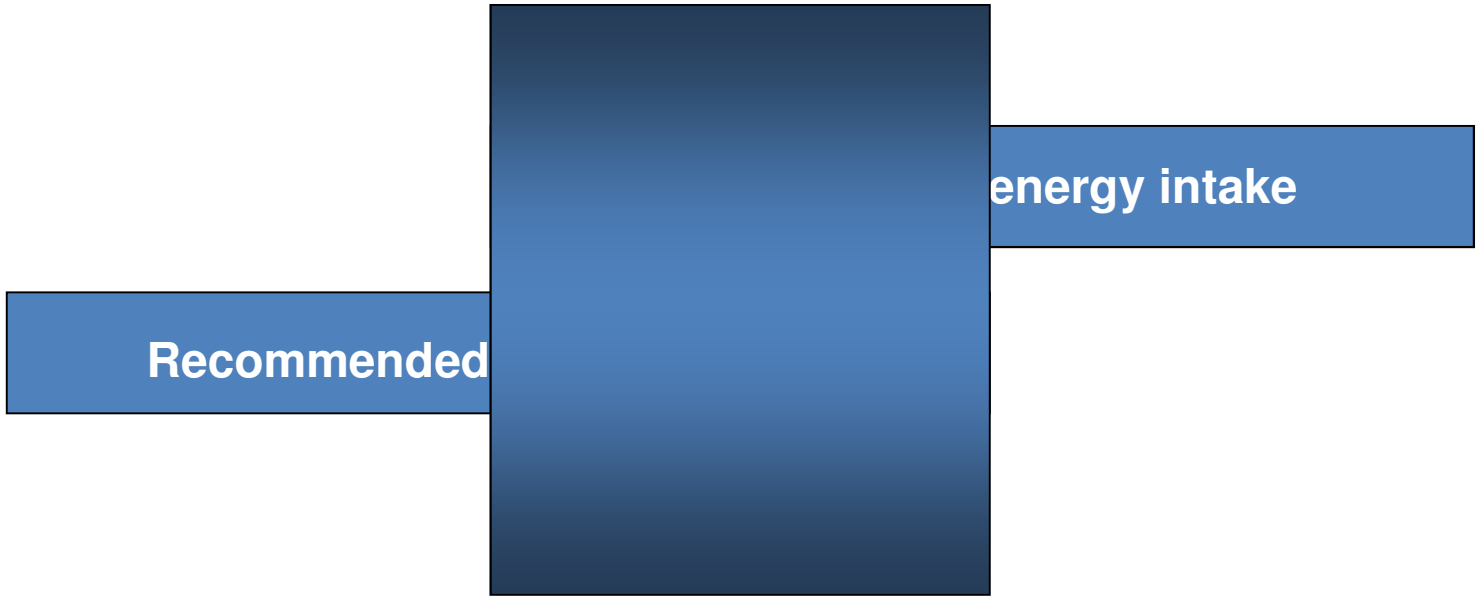
[1]Children's National, Washington, United States, [2]University of Maryland Baltimore County, Baltimore, United States, [3]Urea Cycle Disorders Consortium, Multiple institutions, United States

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

Background

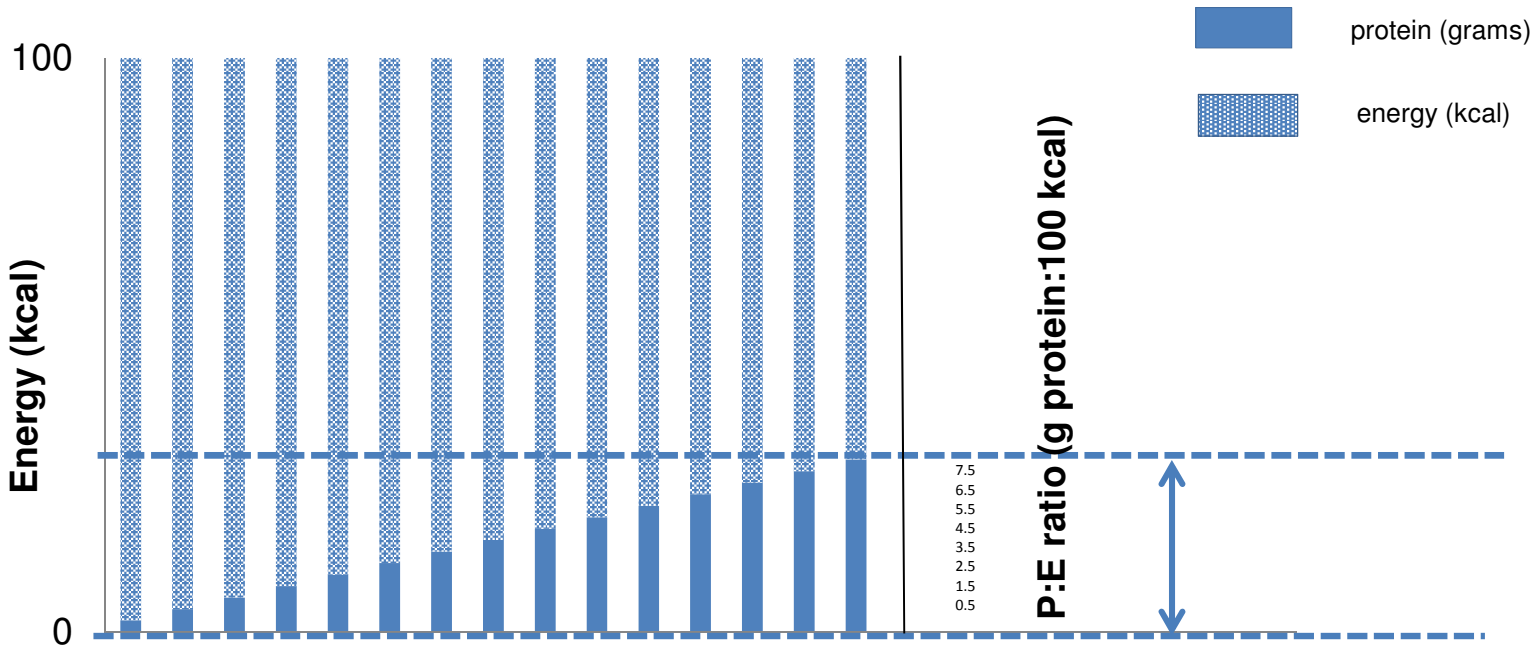
- Protein requirements are based on:
  - Adequate energy intake in order to
    - Utilise protein efficiently
    - Maintain Nitrogen balance
    - Allows tissue synthesis & growth
  - Protein of high & low biological value sources for
    - digestibility
    - amino acid content & ratios

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: • 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 • Growth • Dietary intake • Body composition • Nutritional bloods DOB: 1995 - 2014	PKU	37
	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 > 3g 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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