centro hospitalar
do Porto

Tratamento dietético nas doenças de intoxicação proteica

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Faculdade de Ciências da Saúde – UFP
CINTESIS – FMUP

Coimbra, 21 de Setembro de 2015

Tratamento dietético

- Alimentação
- Dieta » Tratamento dietético → cálculo da dieta
- **Necessidades nutricionais** do doente?

- Qual a doença?
- Qual a situação clínica?

Que recomendações nutricionais?

Rocha JC, 2015

Uso da dieta como terapêutica

- Pressupostos:
  - Prescrição assente nas necessidades nutricionais do doente
  - Dieta tem teor nutricional definido
  - Nenhuma dieta é definitiva!
  - Pediatria: variação das necessidades nutricionais
  - Situação clínica / evolução

O melhor tratamento dietético não se prescreve, monitoriza-se!

Rocha JC, 2015

Estratégia do tratamento dietético

- Controlo do substrato!
  - Restrição, exclusão ou suplementação.

Desafios!

- Uso prolongado de determinadas dietas: consequências?
- Importância do balanço energético.
- Favorecer o crescimento sem fomentar obesidade!
- Osmolaridade das soluções.

Sanjurjo P and Baldellou A. Diagnóstico y tratamiento de las enfermedades metabólicas hereditárias. 4ª Edicion. (2014)

Proteína / aminoácidos

- Como definir as necessidades proteicas?

1. Quais as necessidades energéticas?
2. Que velocidade de crescimento?
3. Tolerância? Genótipo?
4. Qualidade proteica.
5. Dieta exequível? Proporção de proteína natural? Fontes alimentares?

Sanjurjo P and Baldellou A. Diagnóstico y tratamiento de las enfermedades metabólicas hereditárias. 4ª Edicion. (2014)

Proteína / aminoácidos

- Diminuição do aporte proteico:

1. Elevação da amónia nas doenças do ciclo da ureia
2. Doenças hereditárias do catabolismo dos aminoácidos
    1. Fenilcetonúria
    2. Leucinose
    3. Tirosinemia
    4. …

Sanjurjo P and Baldellou A. Diagnóstico y tratamiento de las enfermedades metabólicas hereditárias. 4ª Edicion. (2014)

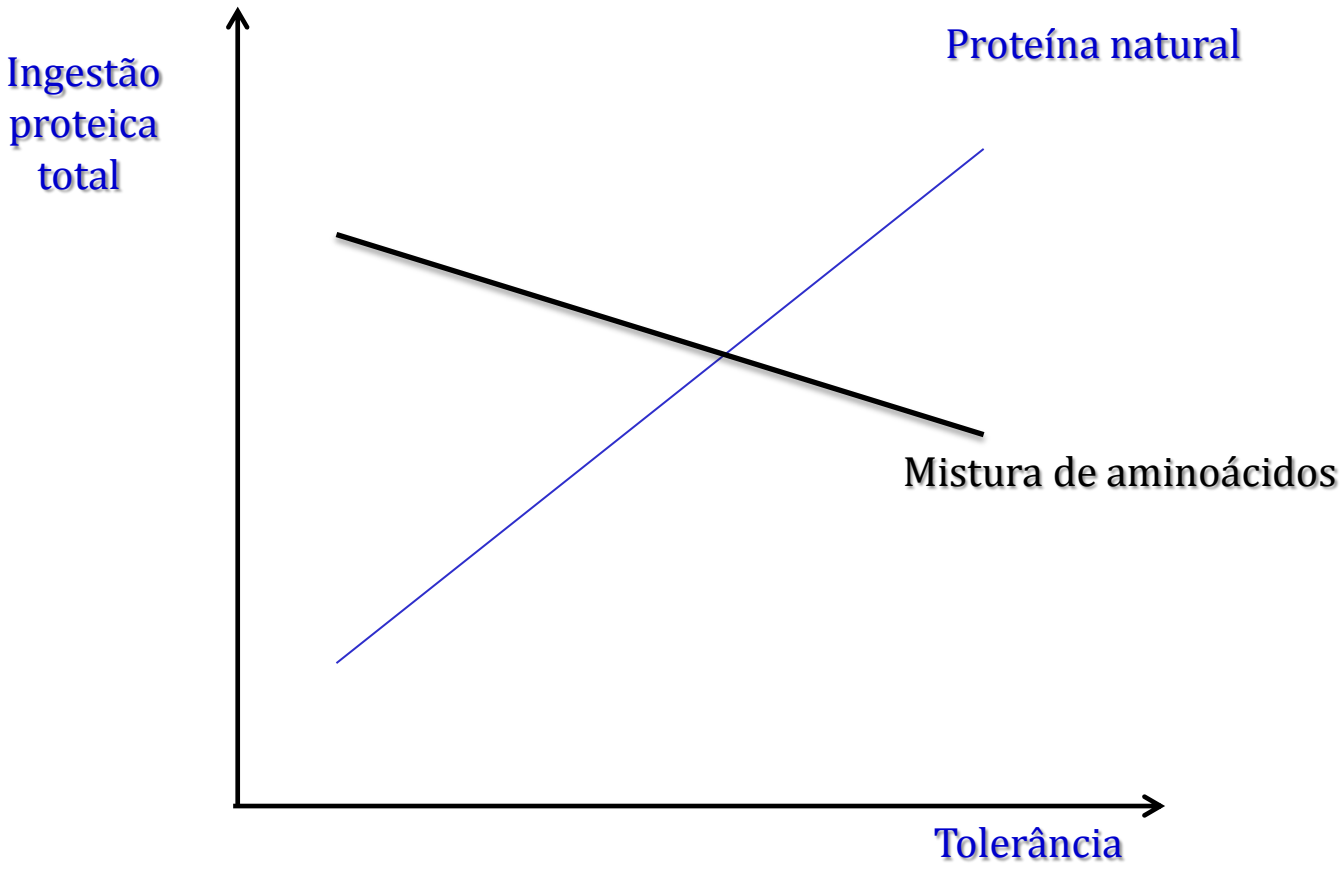
Cuidados na restrição proteica

1. Necessidades mínimas são satisfeitas?
2. Razão azoto / energia respeitada?
3. Quais as fontes proteicas?
4. Dar preferência a alimentos!
5. Biodisponibilidade das misturas de aminoácidos.

Sanjurjo P and Baldellou A. Diagnóstico y tratamiento de las enfermedades metabólicas hereditárias. 4ª Edicion. (2014)

Rocha JC, 2015

Ingestão proteica total



MacDonald. J Inherit Metab Dis. 27:363-371, 2004

MacDonald A. Clinical paediatric dietetics, 2007

Objectivos da mistura de aminoácidos

- Melhorar tolerância – controlo metabólico
- Aumentar a retenção de azoto
- Garantir aporte em micronutrientes
- Manter o equilíbrio no transporte através da barreira hemato-encefálica (BHE)

Rocha JC, 2015

MacDonald A. Clinical paediatric dietetics, 2007

Tratamento dietético inicial

1. Leite materno?
2. Severidade do diagnóstico bioquímico.
3. Pausa na ingestão de proteína natural.
4. Início imediato da mistura de aminoácidos?
5. Fontes de energia!

Rocha JC, et al. Acta Pediatr Port, 2007

Esquema prático – lactentes

MAA +
Energia

+

Proteína
natural

8 x por dia

OU

6 x / dia
+
2 x leite materno (noite)

MAA + Energia +
proteína natural

8 x/ dia

Rocha JC, 2015

Rocha JC, *et al*. Acta Pediatr Port, 2007

Diversificação alimentar

DIETA PARA FENILCETONÚRIA

TABELA DE EQUIVALENTES DE FENILALANINA

PESO DO ALIMENTO **EM GRAMAS** QUE FORNECE **20 mg FEN** = **1 PARTE**

ALIMENTO (Pronto a comer ou cozinhar)	PESO (g)	ALIMENTO (Pronto a comer ou cozinhar)	PESO (g)	ALIMENTO (Pronto a comer ou cozinhar)	PESO(g)
BATATA		Cogumelos cozidos#	43	Pimento vermelho cru#	77
Batata assada com casca$^{\Delta}$	18	Cogumelos lata (escorridos)*	21	Quiabo cozido#	31
Batata assada no forno$^{\Delta}$	17	Cogumelos frescos crus#	24	Quiabo cru#	27
Batata cozida nova$^{\Delta}$	29	Cogumelos fritos$^{\Delta}$	17	Quiabo frito#	18
Batata crua$^{\Delta}$	22	Courgette cozida#	38	Rabanetes crus#	110
Batata doce cozida$^{\Delta}$	49	Courgette crua#	43	Salsa crua*	25
Batata doce crua$^{\Delta}$	43	Courgette frita#	30	Tomate cru$^{\Delta}$	133
Batata em Puré$^{\Delta}$**	31	Couve Branca cozida$^{\Delta}$	77	Tomate em lata$^{\Delta}$	105
Batata frita à Inglesa$^{\Delta}$	12	Couve Branca crua$^{\Delta}$	34	Tomate frito$^{\Delta}$	111
Batata frita congelada crua$^{\Delta}$	21	Couve Coração crua*	51	Vagem (feijão verde)$^{\Delta}$	63
		Couve de Bruxelas cozida$^{\Delta}$	20		

Rocha JC, 2015

Short Communication

European Journal of Clinical Nutrition **68**, 401-403 (March 2014) | doi:10.1038/ejcn.2013.272

Unrestricted fruits and vegetables in the PKU diet: a 1-year follow-up

C Rohde, U Mütze, S Schulz, A G Thiele, U Ceglarek, J Thiery, A S Mueller, W Kiess and S Beblo

Phenylketonuria (PKU) therapy demands phenylalanine (Phe) calculation. In most countries, almost all food is taken into account, even fruits and vegetables. We investigated whether unrestricted consumption of fruits and vegetables negatively influences metabolic control. Nineteen PKU children (2–10 years) started with 2 weeks of free or restricted fruit and vegetable intake. After 2 weeks, the regime changed from free to restricted or restricted to free (cross-over design). Over the first 4 weeks, dried blood Phe concentration was measured, fruit and vegetable consumption recorded and nutrient intake calculated from diet records. Thereafter the diet was changed to free use of fruits and vegetables for all patients. Six and 12 months later, diet and Phe concentrations were monitored. Median Phe intake increased significantly by 65 mg/day (week 4, P<0.001), 68 mg/day (month 6, P<0.001) and 70 mg/day (month 12, P<0.001). Dried blood Phe concentrations remained stable (P=0.894), as did the frequency of Phe concentrations above the recommended range (P=0.592). In conclusion, PKU diet liberalization for fruits and vegetables seems unproblematic.

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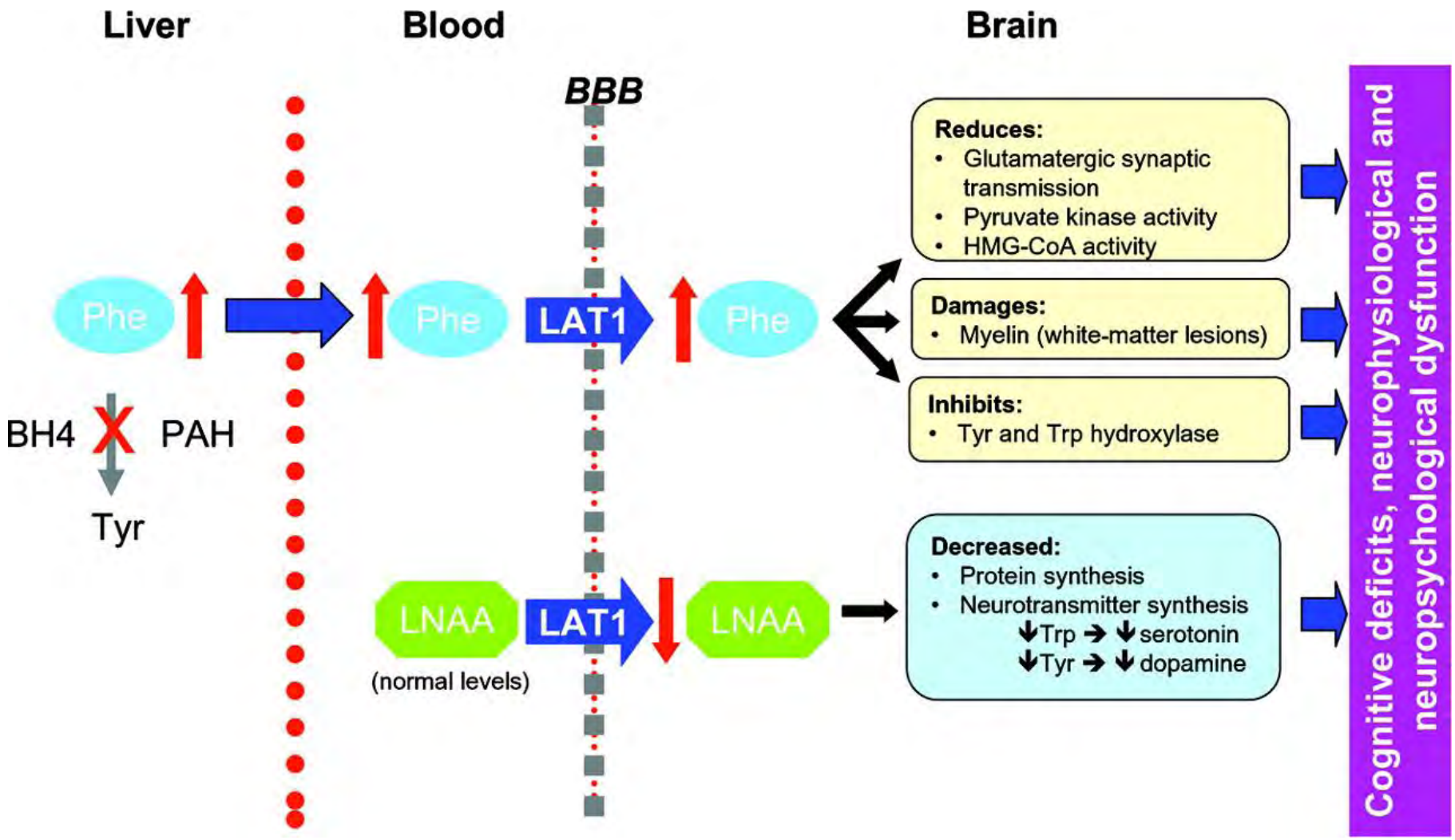
SEARCH PUBMED FOR

- C Rohde
- U Mütze
- S Schulz
- A G Thiele
- U Ceglarek
- J Thiery
- more authors of this article

Rocha JC, 2015

Na PKU, ter apenas em conta a fen?



Feillet F, et al. Pediatrics 2010;126:333-341

Rocha JC, 2015

Prescrição da mistura de aminoácidos na PKU

1º ano de vida	3 $g.kg^{-1}.dia^{-1}$
Infância	2 $g.kg^{-1}.dia^{-1}$
Adultos	1 $g.kg^{-1}.dia^{-1}$

Walter JH, Lee PJ and Burgard P. Inborn Metabolic Diseases, 2006

Será necessário?

Até aos 2 anos	3 $g.kg^{-1}.dia^{-1}$
Após os 2 anos	2 $g.kg^{-1}.dia^{-1}$

Medical Research Council Working Party of Phenylketonuria. Arch Dis Child, 1993

Rocha JC, *et al*. Acta Pediatr Port, 2007

Alimentos especiais hipoproteicos

Food item	Special low protein *Nutrition facts (g/100g)*		Regular equivalent * *Nutrition facts (g/100g)*	
"Biscuits Sablés"	Energy	474 kcal	Energy	436
	CHO (sugars)	78.9 (18.7)	CHO (sugars)	72 (21.5)
	FAT (saturated)	17.3 (9.0)	FAT (saturated)	12.2 (5.9)
	PROT	0.5	PROT	8.4
Pasta	Energy	348	Energy	354
	CHO (sugars)	84.3	CHO (sugars)	70
	FAT (saturated)	0.6	FAT (saturated)	1.8
	PROT	0.3	PROT	12.4
Cookies cacao chips	Energy	466	Energy	466
	CHO (sugars)	78.8 (17.8)	CHO (sugars)	65.4 (24)
	FAT (saturated)	17.7 (7)	FAT (saturated)	19.8 (12.4)
	PROT	0.55	PROT	5.7
Crackers	Energy	448	Energy	451
	CHO (sugars)	78 (1.5)	CHO (sugars)	61 (1.4)
	FAT (saturated)	15 (7)	FAT (saturated)	17.8 (7.6)
	PROT	0.4	PROT	9.8
Bread	Energy	355	Energy	289
	CHO (sugars)	87.4 (5.1)	CHO (sugars)	57.3 (2.1)
	FAT (saturated)	0.42 (0.23)	FAT (saturated)	2.2 (0.5)
	PROT	0.31	PROT	8.4

* INSA. Portuguese Food Composition Table. 2006

Rocha JC, 2015

Recomendações nutricionais na Leucinose

Nutrient	Recommendation	Source
LEU	Sufficient intake to allow adequate protein synthesis for growth, repair and health maintenance and to achieve LEU concentrations in recommended treatment range. LEU allowance is also dependent on residual BCKD activity, age, weight, sex, life stage and health of the individual with MSUD.	• Intact protein (PRO) *In infants*: breast milk or infant formula with known LEU content *In children and adults*: foods such as fruits/vegetables and some grains/cereals that are typically low in protein and for which there is a known LEU content
PRO	DRI [a] Plus additional 20–40% if an amino acid–based medical food is used[b]	• Intact PRO (as above) • BCAA-free medical food [c]
VAL, ILE	VAL and ILE are essential amino acids and may need to be supplemented when BCAA are restricted to achieve appropriate LEU blood concentrations. To promote anabolism of LEU, when LEU blood concentrations are high, additional supplementation of VAL and ILE is often required	• Intact PRO • Supplemental VAL, ILE [d]
Energy	DRI [a]	• Intact PRO • BCAA-free medical food • Free foods [e] • Modified low-PRO food [f]
Other nutrients, minerals and vitamins [f]	DRI [a]	• Intact PRO • BCAA-free medical food • Supplemental nutrients, vitamins and minerals [g]

Rocha JC, 2015

Frazier DM, et al. Mol Genet Metab, 2014; 112:210-7

Leucinose

DESCOMPENSAÇÕES METABÓLICAS

Situações de catabolismo (infecções, vacinas, erros alimentares...)

redução do aporte de leucina
suplementos energéticos – cuidado com osmolaridade!
hospitalização
depuração exógena se:
- deterioração neurológica / clínica
- ↓ [Leu] < 500 μmol/L nas 24h

Rocha JC, 2015

Leucinose

DESCOMPENSAÇÕES METABÓLICAS

Situações de catabolismo (infecções, vacinas, erros alimentares...)

redução do aporte de leucina
suplementos energéticos – cuidado com osmolaridade!
hospitalização
depuração exógena se:
- deterioração neurológica / clínica
- ↓ [Leu] < 500 μmol/L nas 24h

Leucina: 80-200 μmol/L

Isoleucina: 40-90 μmol/L

Valina: 200-425 μmol/L

Prognóstico

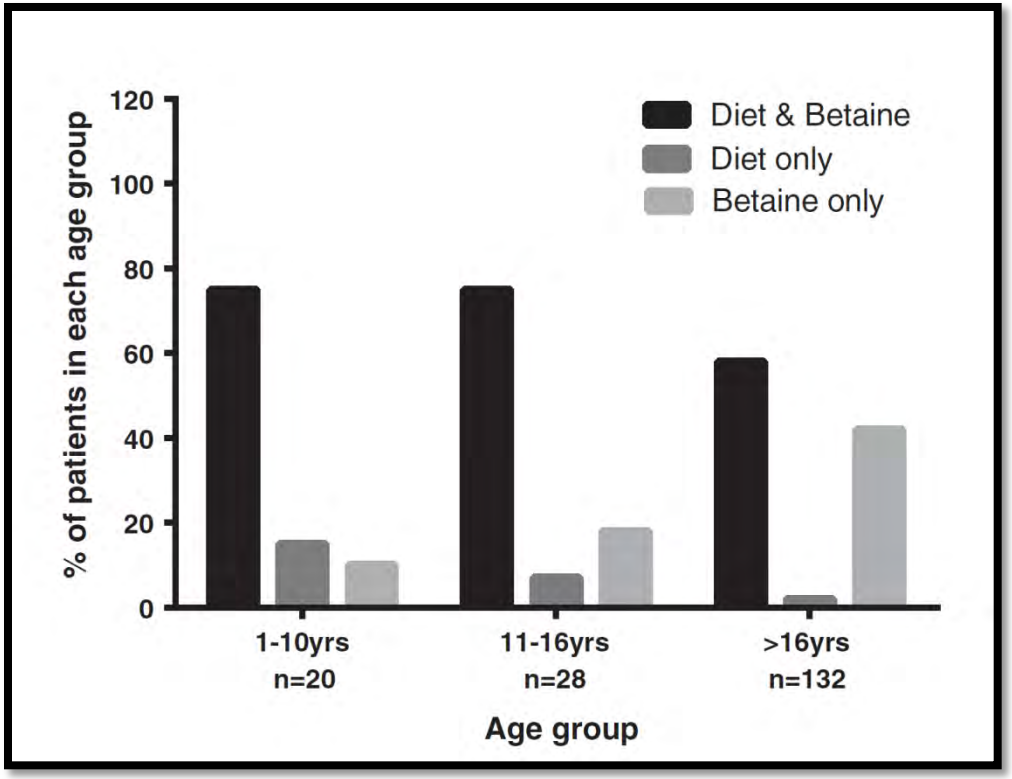
Rocha JC, 2015

Acosta PB. Nutrition Management of Patients with Inherited Metabolic Disorders, 2010

Molecular Genetics and Metabolism 110 (2013) 454–459

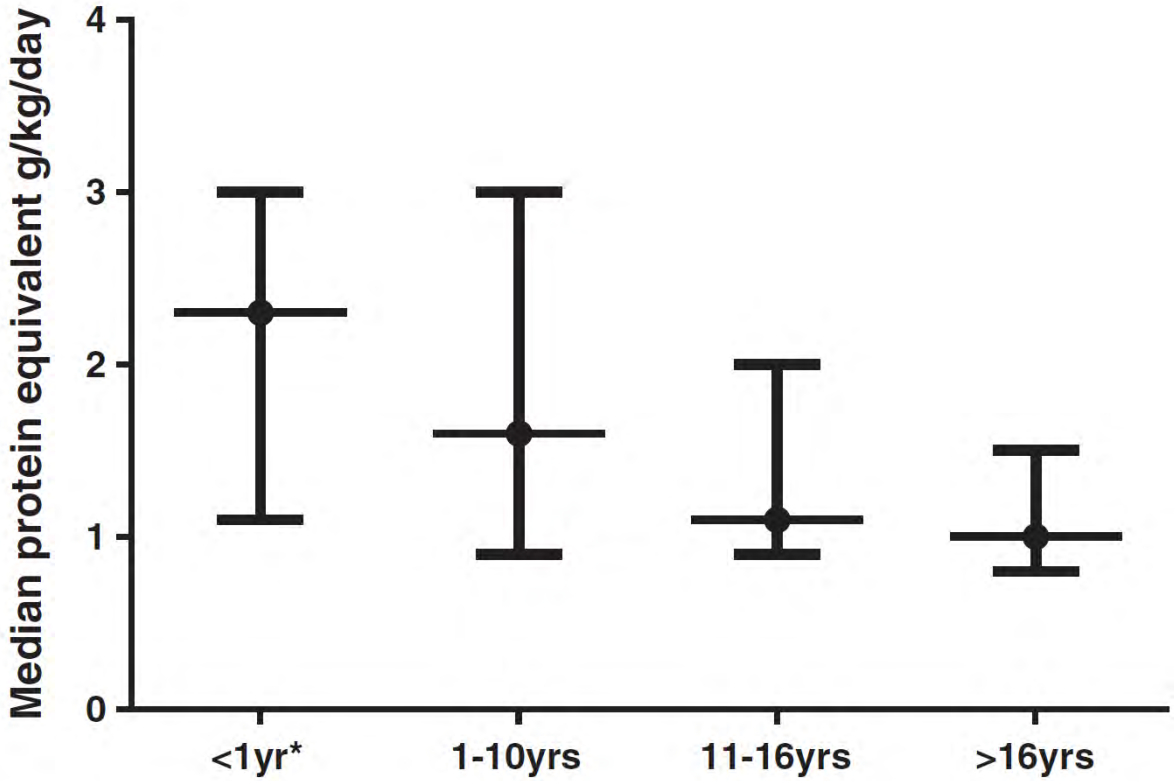
Dietary practices in pyridoxine non-responsive homocystinuria: A European survey

S. Adam [a], M.F. Almeida [b], E. Carbasius Weber [c], H. Champion [d], H. Chan [e], A. Daly [f], M. Dixon [g], K. Dokoupil [h], D. Egli [i], S. Evans [f], F. Eyskens [j], A. Faria [k], C. Ferguson [l], P. Hallam [m], M. Heddrich-Ellerbrok [n], J. Jacobs [o], C. Jankowski [p], R. Lachmann [e], R. Lilje [q], R. Link [r], S. Lowry [s], K. Luyten [j], A. MacDonald [f,*], C. Maritz [e], E. Martins [t], U. Meyer [u], E. Müller [v], E. Murphy [e], L.V. Robertson [w], J.C. Rocha [b], I. Saruggia [x], P. Schick [v], J. Stafford [g], L. Stoelen [q], A. Terry [y], R. Thom [z], T. van den Hurk [c], M. van Rijn [aa], A. van Teefelen-Heithoff [ab], D. Webster [p], F.J. White [ac], J. Wildgoose [ad], H. Zweers [ae]



Rocha JC, 2015

Molecular Genetics and Metabolism 110 (2013) 454–459



	<1yr*	1-10yrs	11-16yrs	>16yrs
Median	2.3	1.6	1.1	1.0
Range	(1.1-3.0)	(0.9-3.0)	(0.9-2.0)	(0.8-1.5)
No. centres	7	18	20	18

Fig. 2. Median protein equivalent prescribed by centres for the different age bands from both dietary protein (methionine) and L-amino acid supplements[#].

Rocha JC, 2015

Adam S, et al. Mol Genet Metab, 2013; 110:454-9

Molecular Genetics and Metabolism 110 (2013) 454–459

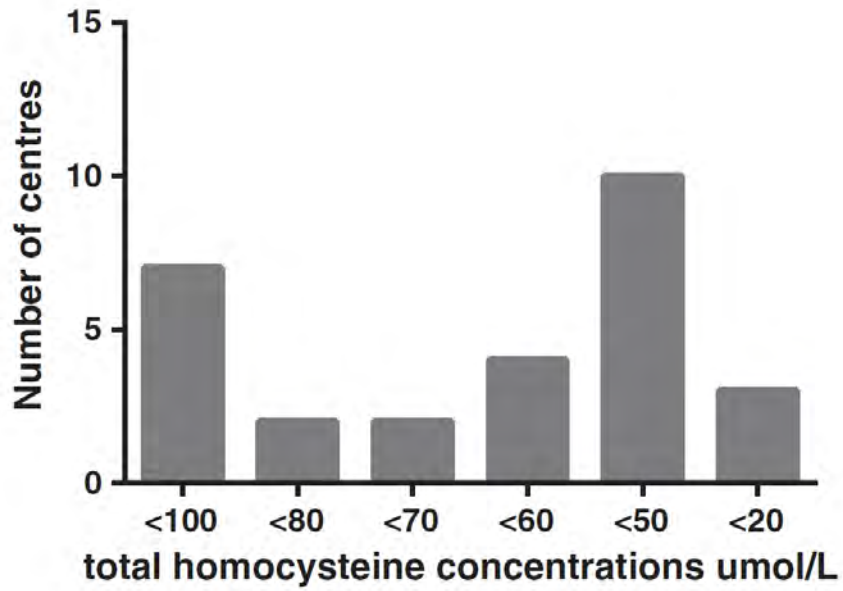


Fig. 3. Biochemical total homocysteine (tHcy) treatment aims by centres (n = 28).

ESTUDO BIOQUÍMICO	RESULTADO	VAL. REFERÊNCIA
SANGUE		
Homocisteína total	↑ 90,8 µmol/L	4,2 - 14,6

VALS, 12 anos

Aminograma?
AACR – Normal?
Aumento da metionina?

Rocha JC, 2015

Adam S, et al. Mol Genet Metab, 2013; 110:454-9

Häberle *et al. Orphanet Journal of Rare Diseases* 2012, **7**:32
http://www.ojrd.com/content/7/1/32

ORPHANET JOURNAL OF RARE DISEASES

REVIEW Open Access

Suggested guidelines for the diagnosis and management of urea cycle disorders

Johannes Häberle[1*], Nathalie Boddaert[2], Alberto Burlina[3], Anupam Chakrapani[4], Marjorie Dixon[5], Martina Huemer[6], Daniela Karall[7], Diego Martinelli[8], Pablo Sanjurjo Crespo[9], René Santer[10], Aude Servais[11], Vassili Valayannopoulos[12], Martin Lindner[13*†], Vicente Rubio[14*†] and Carlo Dionisi-Vici[8*†]

Evidência dos estudos: <u>raramente excede nível C</u> (*case-reports*, séries de doentes).

Todavia….

é um guia para o diagnóstico e tratamento das DCU.

Rocha JC, 2015

Hiperamoniemia aguda

Hiperamoniemia aguda» **EMERGÊNCIA!**

- Hospitais pediátricos referenciados.
- Medicação de primeira linha disponível.
- Protocolos definidos por escrito.

Doente em crise de hiperamoniemia transferido para centro de referência após:

1. **Parar ingestão proteica.**
2. **Início de glicose EV a 10%.**
3. **Início da medicação de primeira linha.**
4. **Colheitas (sangue e urina) para efeitos de diagnóstico sem atrasar terapêutica!**

Häberle J, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders. Orphanet Journal of Rare Diseases 2012, 7:32

Mau prognóstico se:

1. **Coma hiperamoniemico há mais de 3 dias.**
2. **Pressão intracraniana claramente aumentada.**
3. **[Amónia] > 1000 uM, embora o impacto no prognóstico dependa da duração da hiperamoniemia.**

Statement #15. Grade of recommendation: C

Total duration of coma and peak ammonia levels are the most relevant factors for neurodevelopmental prognosis. More studies are needed to identify other potential contributing factors.

Häberle J, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders. Orphanet Journal of Rare Diseases 2012, 7:32

Métodos dialíticos

Statement #17. Grade of recommendation: C-D

In neonates and children with symptomatic hyperammonemia, dialysis should be carried out when ammonia exceeds 500 µmol/L or when there is no response within four hours after starting medical treatment.

Häberle J, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders. Orphanet Journal of Rare Diseases 2012, 7:32

Rocha JC, 2015

Intervenção nutricional na fase aguda

1. **Minimizar temporariamente a ingestão proteica (azoto).**
2. **Prevenir catabolismo proteico endógeno.**
3. **Garantir aporte energético adequado (polímeros de glicose ou glicose EV + insulina, em função da tolerância).**

Table 6 Emergency regimen for protein-free feeding in infants and children

Age	Glucose polymer concentration (% carbohydrates)	Energy/100ml		Suggested daily intake	Feeding frequency
		kcal	kJ		
up to 6 m	10	40	167	150ml/kg	2 to 3 hourly oral/bolus
7-12 m	10-15	40-60	167-250	120ml/kg	day and night
1 y	15	60	250	1200ml	or continuous tube
2-9 y	20	80	334	Estimate as indicated[a]	feeds using enteral
>10 y	25	100	418	Estimate as indicated[a]	feeding pump

Adapted from Clinical Pediatric Dietetics [106]. *Grade of recommendation, C-D.*
[a] For children >10 kg emergency regimen fluid requirements can be calculated as:
11–20 kg: 100ml/kg for the first 10 kg, plus 50ml/kg for the next 10 kg.
>20 kg: 100ml/kg for the first 10 kg, plus 50ml/kg for the next 10 kg, plus 25ml/kg thereafter up to a maximum of 2500ml/day.

Häberle J, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders. Orphanet Journal of Rare Diseases 2012, 7:32

Intervenção nutricional na fase aguda

Statement #20. Grade of recommendation: D

For treatment of acute hyperammonemia it is crucial to promote and maintain anabolism by infusing high-dose glucose plus lipids (if a fatty acid oxidation disorder has been excluded). Protein should be reintroduced when ammonia returns to <100 μmol/L. Ideally the period of protein-free nutrition should not exceed 24–48 hours.

Häberle J, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders. Orphanet Journal of Rare Diseases 2012, 7:32

Rocha JC, 2015

Ingestão proteica nos doentes com défice em OTC

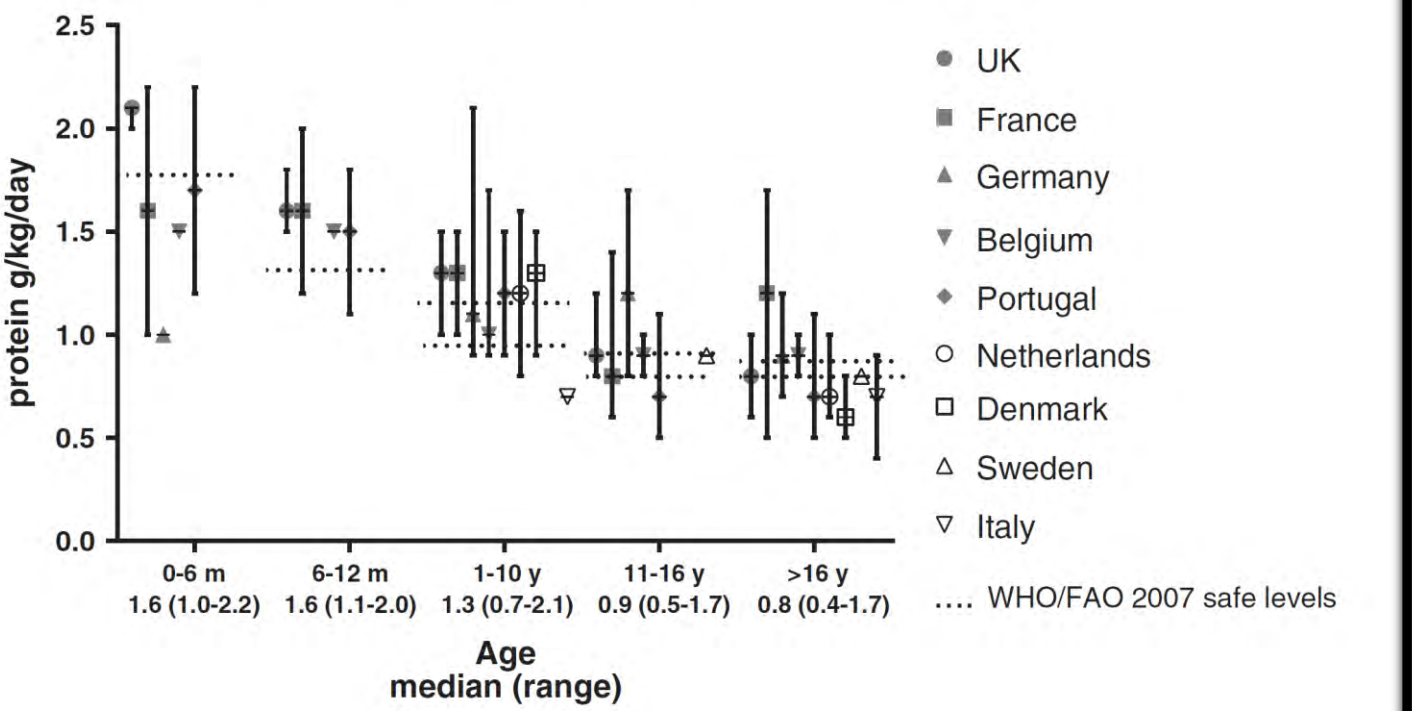


Fig. 1. OTC: Median protein intake (g/kg) for different age groups by country.

Rocha JC, 2015

O trabalho em equipa...

Molecular Genetics and Metabolism xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Molecular Genetics and Metabolism

journal homepage: www.elsevier.com/locate/ymgme

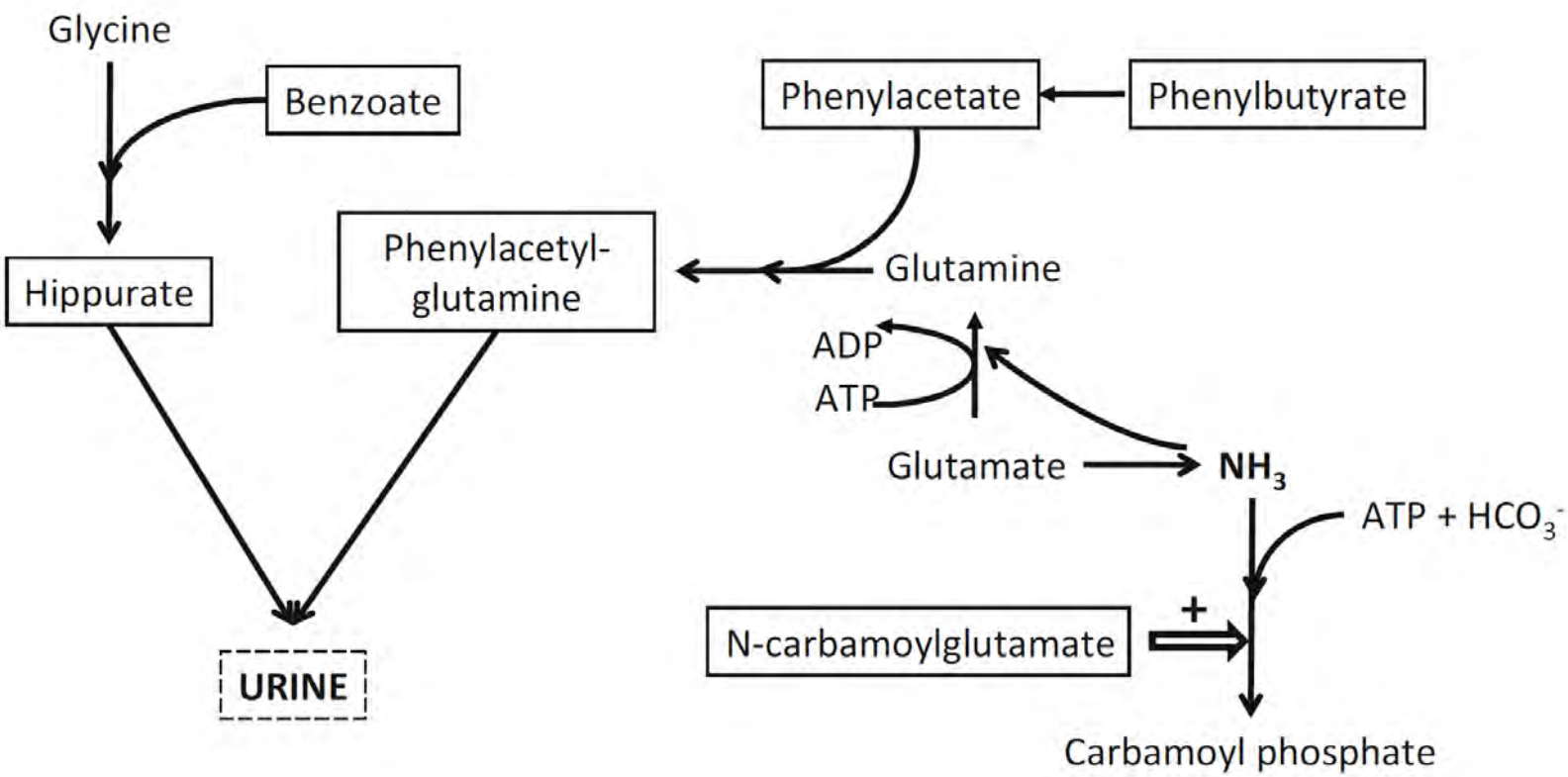
Sodium phenylbutyrate decreases plasma branched-chain amino acids in patients with urea cycle disorders

Lindsay C. Burrage [a,1], Mahim Jain [a,1], Laura Gandolfo [b], Brendan H. Lee [a,c], Members of the Urea Cycle Disorders Consortium [2], Sandesh C.S. Nagamani [a,*]

[a] Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, TX, USA
[b] University of South Florida, Tampa, FL, USA
[c] Howard Hughes Medical Institute, Houston, TX, USA

Rocha JC, 2015

Drogas excretoras do azoto



E a dieta???
Contexto da ingestão proteica??

Saudubray, van den Berghe, Walter. *Inborn Metabolic Diseases*. 5th Edition (2012).

Rocha JC, 2015

Acidúria glutárica tipo 1 - Recomendações

Quadro II – Recomendações e cuidados primários no domicílio numa fase aguda. Adaptado de Kölker *et al* [3].

Idade (anos)	Maltodextrinas / glicose %	Maltodextrinas / glicose (kcal/100mL) via oral	Volume em mL por dia (via oral)
A. Maltodextrinas / glicose			
0-1	10	40	Mínimo 150/kg
1-2	15	60	120/kg
2-6	20	80	1200-1500
>6	Manter recomendações anteriores com adaptação individual.		
B. Ingestão proteica			
Proteína natural	Suspender (se faz mistura de aminoácidos) ou reduzir a 50% (se não faz mistura de aminoácidos) a prescrição anterior com reintrodução gradual após 24 a 48 horas.		
Mistura de aminoácidos	Se tolerado, administrar a mistura de aminoácidos de acordo com a terapêutica de manutenção: 0.8-1.3g/kg.		
C. Fármacos			
L-carnitina	Dobrar ingestão até 200mg.kg^{-1}.dia^{-1}.		
Antipiréticos	Se febre > 38,5°C: ibuprofeno (10-15mg/kg por dose, em 3 a 4 tomas por dia).		

Rocha JC, 2015

Recomendações nutricionais

Quadro I – Recomendações nutricionais para a AGI. Acima dos 6 anos de idade recomenda-se evitar o aporte excessivo de proteína natural, optando por alimentos com baixo teor em lisina.

		0-6 meses	7-12 meses	1-3 anos	4-6 anos	>6 anos	adultos
Lisina	$mg.kg^{-1}.dia^{-1}$	100[a]	90 [a]	60-80 [a]	50-60 [a]	- [c]	- [c]
Triptofano	$mg.kg^{-1}.dia^{-1}$	20 [a]	17 [a]	13-17 [a]	13 [a]	- [c]	- [c]
Proteína natural	$g.kg^{-1}.dia^{-1}$	1.3-1.4 [a]	1.3-1.5 [a]	1.3-1.4 [a]	1.1-1.3 [a]	1.1-1.5 [b]	1.0 [b]
Mistura de a.a.	$g.kg^{-1}.dia^{-1}$	0.8-1.3 [a]	0.8-1.0 [a]	0.8 [a]	0.8 [a]	- [c]	- [c]
Energia	$kcal.kg^{-1}.dia^{-1}$	82-115 [a]	80-95 [a]	82-95 [a]	78-90 [a]	60-70 [b]	40-50 [b]
L-Carnitina	$mg.kg^{-1}.dia^{-1}$	100 [b]	100 [b]	100 [a]	50-100 [b]	50-100 [b]	50 [b]
Micronutrientes	%[d]	≥100 [a]	≥100 [a]	≥100 [a]	≥100 [a]	>100 [a]	- [c]

a - Adaptado de Kölker *et al* [3]; b - Adaptado de Hoffmann GF [8]. c - Não disponível. d - De acordo com as DRI's, Dietary Reference Intakes, Institute of Medicine.

Rocha JC, 2015

Molecular Genetics and Metabolism 104 (2011) 93–106

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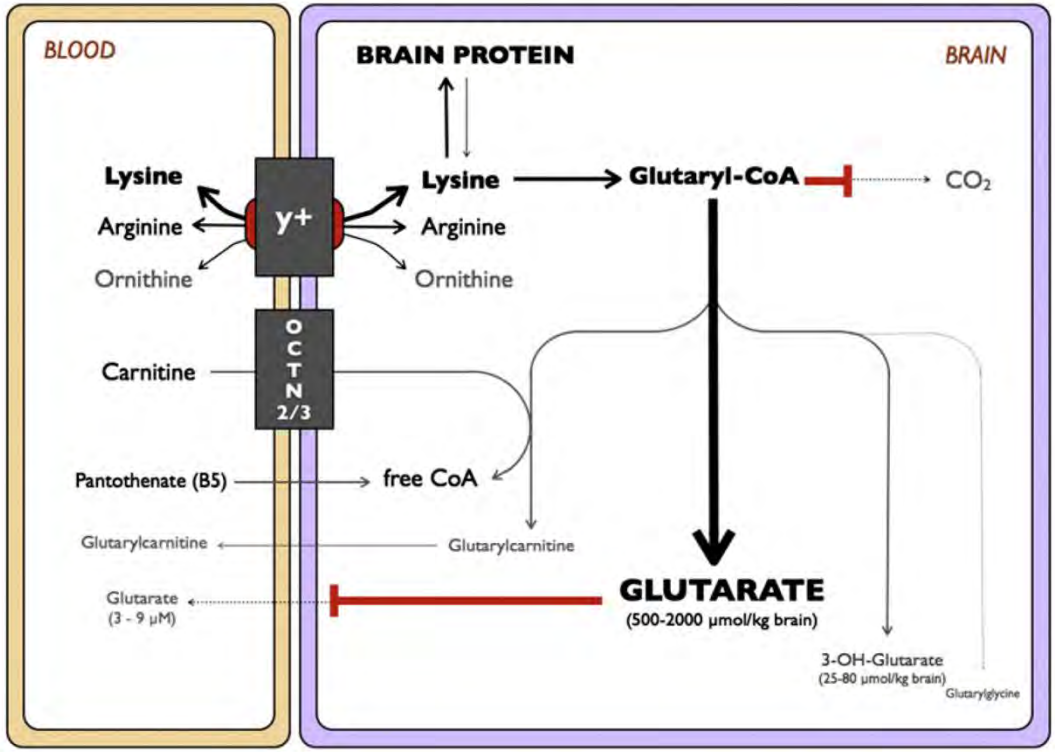
Molecular Genetics and Metabolism

journal homepage: www.elsevier.com/locate/ymgme

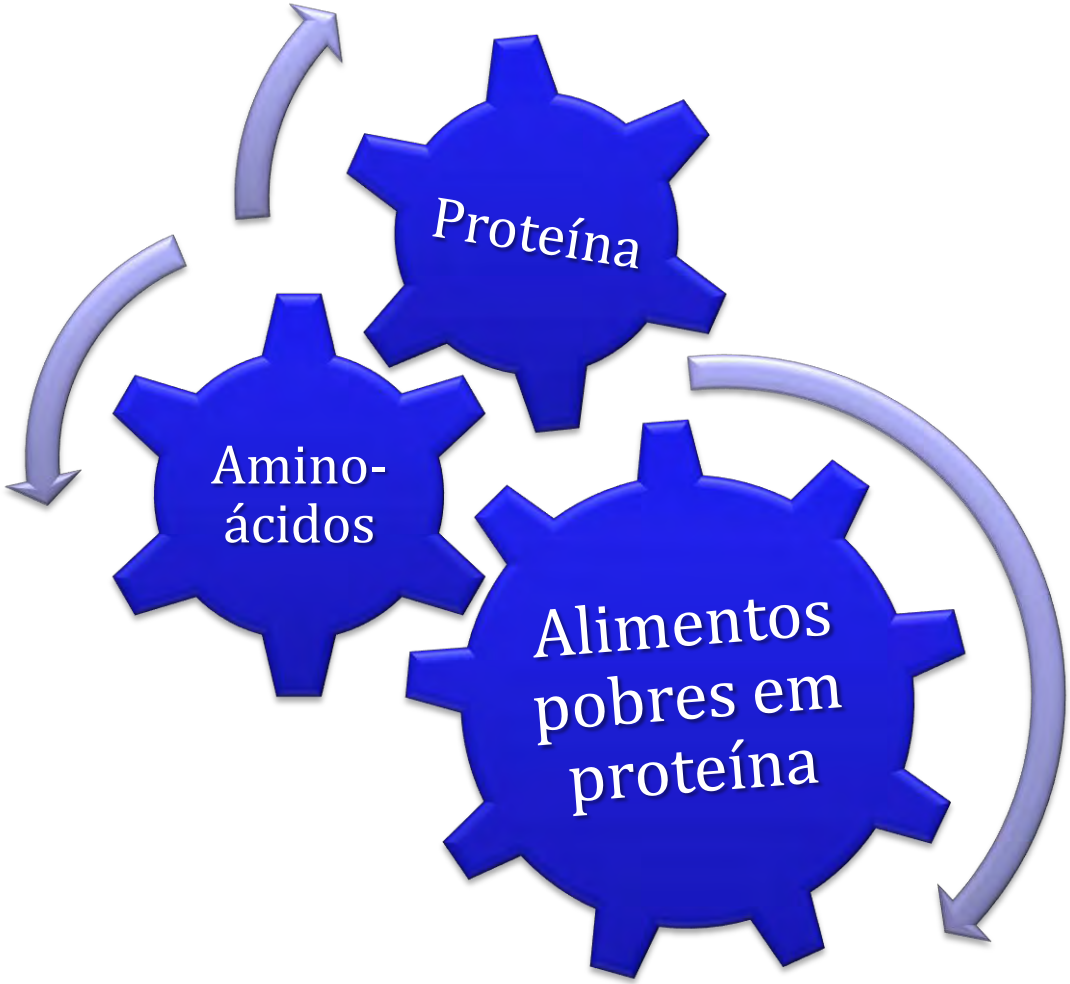
Safety, efficacy and physiological actions of a lysine-free, arginine-rich formula to treat glutaryl-CoA dehydrogenase deficiency: Focus on cerebral amino acid influx

Kevin A. Strauss [a,b,c,*], Joan Brumbaugh [b,1], Alana Duffy [d], Bridget Wardley [d,e,1], Donna Robinson [a], Christine Hendrickson [a], Silvia Tortorelli [f], Ann B. Moser [g], Erik G. Puffenberger [a,b,c], Nicholas L. Rider [a,c], D. Holmes Morton [a,b,c]



Rocha JC, 2015

Padrão alimentar nas Doenças Hereditárias do Metabolismo Proteico



Rocha JC, 2015

Molecular Genetics and Metabolism 115 (2015) 17–22

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Practices in prescribing protein substitutes for PKU in Europe: No uniformity of approach

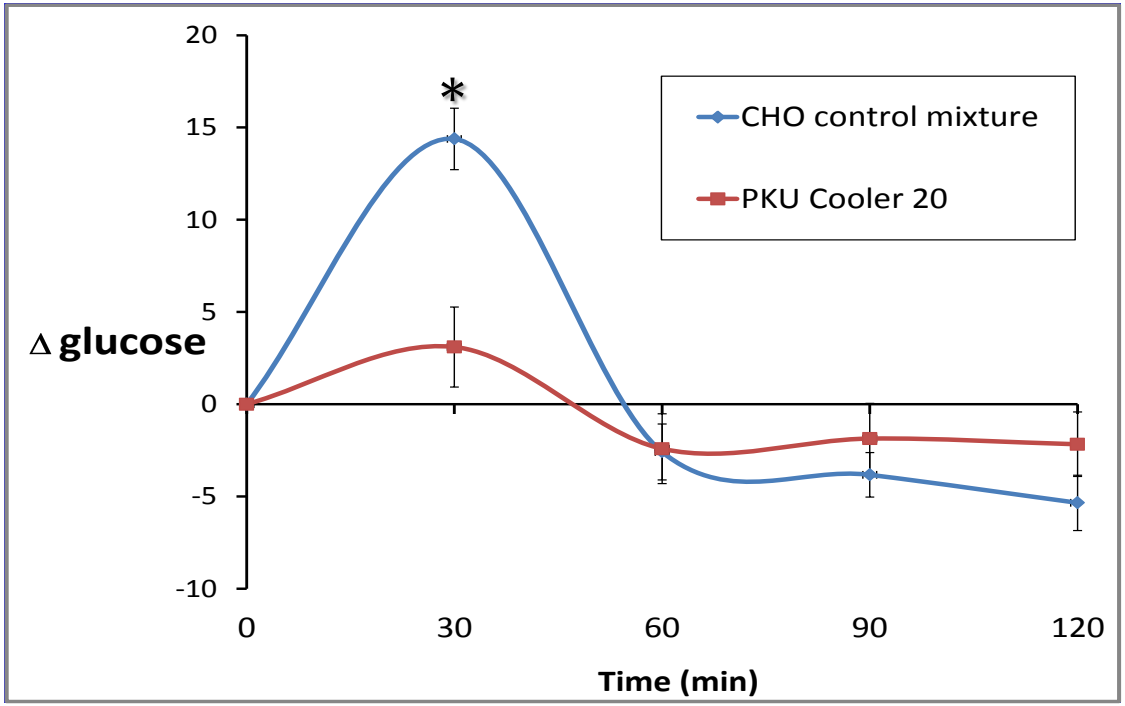
A. Aguiar [a], K. Ahring [b], M.F. Almeida [c,d], M. Assoun [e], A. Belanger Quintana [f], S. Bigot [g], G. Bihet [h], K. Blom Malmberg [i], A. Burlina [j], T. Bushueva [k], A. Caris [l], H. Chan [m], A. Clark [n], S. Clark [o], B. Cochrane [p], K. Corthouts [q], J. Dalmau [r], M. Dassy [s], A. De Meyer [t], B. Didycz [u], M. Diels [v], K. Dokupil [w], S. Dubois [e], K. Eftring [x], J. Ekengren [x], C. Ellerton [y], S. Evans [z], A. Faria [aa], A. Fischer [ab], S. Ford [ac], P. Freisinger [ab], M. Giżewska [ad], H. Gokmen-Ozel [ae], J. Gribben [m], F. Gunden [af], M. Heddrich-Ellerbrok [ag], S. Heiber [ah], C. Heidenborg [ai], C. Jankowski [aj], R. Janssen-Regelink [ak], I. Jones [t], C. Jonkers [al], M. Joerg-Streller [am], K. Kaalund-Hansen [y], E. Kiss [an], A.M. Lammardo [ao], K. Lang [ap], D. Lier [ab], R. Lilje [aq], S. Lowry [ar], K. Luyten [t], A. MacDonald [z,*], U. Meyer [as], D. Moor [at], A. Pal [au], M. Robert [av], L. Robertson [aw], J.C. Rocha [c,ax,ay], C. Rohde [az], K. Ross [ba], S. Saruhan [ae], E. Sjöqvist [bb], R. Skeath [bc], L. Stoelen [aq], N.M. Ter Horst [bd], A. Terry [be], C. Timmer [bf], N. Tuncer [bg], K. Vande Kerckhove [q], L. van der Ploeg [bh], M. van Rijn [bi], F.J. van Spronsen [bi], A. van Teeffelen-Heithoff [bj], A. van Wegberg [ak], K. van Wyk [m], C. Vasconcelos [bk], I. Vitoria [r], J. Wildgoose [bl], D. Webster [aj], F.J. White [bm], H. Zweers [ak]

Rocha JC, 2015

Impact of amino acid ingestion on glucose metabolism

- **Objective**: to compare the effect on glycaemia of drinking a PKU Cooler 20® or a solution containing its sugars, measuring glycaemia at 0, 30, 60, 90 and 120 min in healthy subjects.

- 29 students from the FMUP (2011)
- 18.8 ± 1.2 y
- BMI 21.7 ± 2.9 kg/m^2
- 55% females



1 pouch of PKU Cooler 20®:
- 24 g of amino acids
- 9.2 g of CHO
  - 7.3 g sucrose
  - 1.2 g starch
  - 0.35 g dextrins
  - 0.35 g glucose

1 cup of 200 mL **water solution** with a mixture that simulate the **CHO content** in one pouch of PKU Cooler 20®:
- 7.3 g sucrose
- 1.74 g Fantomalt®
- 0.24 g glucose.

Biochemistry Department, Faculty of Medicine, University of Porto
2011

Rocha JC, 2015

No differences regarding body composition between patients and controls

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journal homepage: www.elsevier.com/locate/ymgme

Early dietary treated patients with phenylketonuria can achieve normal growth and body composition

Júlio C. Rocha [a,*], Francjan J. van Spronsen [b], Manuela F. Almeida [a], Elisabete Ramos [c,d], João T. Guimarães [d,e,f], Nuno Borges [g]

	Patients (N = 89)	Controls (N = 78)	*p*
Fat mass (%) [median [P25–P75]]	22.0 [14.4–28.9]	23.1 [16.3–28.8]	0.672
Fat free mass (%) [median [P25–P75]]	78.0 [71.1–85.7]	77.0 [71.2–83.7]	0.656
Muscular mass (%) [median [P25–P75]]	48.3 [43.0–53.3]	46.7 [43.5–53.2]	0.572
Body cell mass index [median [P25–P75]]	7.4 [6.6–8.7]	7.6 [6.8–8.9]	0.251
Phase angle [median [P25–P75]]	5.9 [5.2–6.5]	6.0 [5.5–6.6]	0.407

Rocha JC, 2015

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Early dietary treated patients with phenylketonuria can achieve normal growth and body composition

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	Patients (N = 89)	Controls (N = 78)	*p*
Age (years) [mean (SD)]	14.4 (6.6)	15.9 (7.1)	0.166
Sex (female)	46%	58%	0.179
Height			
Height z-score [mean (SD)] (<19 y) (n = 63)	−0.06 (0.94)	0.16 (1.03)	0.301
Height [median [P25–P75]] (≥19 y) (n = 26)	160.5 [151.9–167.5]	168.0 [159.2–174.8]	0.017
Fat mass (%) [median [P25–P75]]	22.0 [14.4–28.9]	23.1 [16.3–28.8]	0.672
Fat free mass (%) [median [P25–P75]]	78.0 [71.1–85.7]	77.0 [71.2–83.7]	0.656
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Rocha JC, 2015

Metabolic syndrome in patient and controls

Comparison of the prevalence of the metabolic syndrome and its components between patients and controls aged >10 years.[a]

	Patients n = 65 (%)	Controls n = 66 (%)	*p*
Central obesity (waist circumference > 90th percentile or adult cut-offs if lower)	24 (36.9)	24 (36.4)	0.999[b]
Raised triglycerides ([TG] ≥ 150 mg/dL)	6 (9.2)	3 (4.5)	0.324[c]
Decreased HDL-cholesterol ([HDL-c] < 40 mg/dL)	17 (26.2)	12 (18.2)	0.374[b]
Raised blood pressure (systolic ≥ 130 mm Hg or diastolic ≥ 85 mm Hg)	0 (0)	5 (7.6)	0.058[c]
Raised glucose ([Glucose] ≥ 100 mg/dL)	0 (0)	3 (4.5)	0.244[c]
Metabolic syndrome (central obesity plus 2 other components)	1 (1.5)	4 (6.1)	0.365[b]

[a] Cut-offs and MetSyn classification were according to the criteria from International Diabetes Federation.

[b] Using Chi-square test.

[c] Using Fisher's Exact test.

Rocha JC, et al. Mol Genet Metab, 2012; 107(4):659-63

Rocha JC, 2015

Marcadores cardiometabólicos em doentes PKU

	DOENTES	CONTROLOS	*p*
Glucose (mg/dL)	80 [75–84]	83 [79–87]	0.005
Insulin (μU/mL)	6.69 [4.73–10.46]	7.99 [4.87–12.20]	0.436
Homeostasis model assessment of insulin resistance	1.42 [0.93–2.08]	1.75 [0.94–2.49]	0.205
Total cholesterol (mg/dL)	150 [129–164.5]	155 [139–175]	0.016
LDL-cholesterol (mg/dL)	78 [62–93]	80 [71–102]	0.100
HDL-cholesterol (mg/dL)	49 [42–59]	57 [48–72]	<0.001
Triglycerides (mg/dL)	72 [54–99]	52 [40–73]	<0.001
Triglycerides/HDL-cholesterol	1.47 [1.04–2.17]	0.92 [0.59–1.30]	<0.001
Total cholesterol/HDL-cholesterol	2.86 [2.46–3.58]	2.68 [2.18–3.11]	0.026
High sensitivity-CRP (mg/L)	0.55 [0.24–1.13]	0.56 [0.29–2.37]	0.304
Uric acid (mg/dL)	3.95 (0.99)	4.35 (1.15)	0.015
Systolic blood pressure (mm Hg)	104.3 (11.8)	110.4 (12.3)	0.003
Diastolic blood pressure (mm Hg)	48.1 (9.4)	51.6 (10.8)	0.027
Heart rate (beats per minute)	72.1 (11.1)	73.0 (16.0)	0.876

Rocha JC, *et al*. Mol Genet Metab, 2012; 107(4):659-63

Rocha JC, 2015

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Minireview

Micronutrient status in phenylketonuria

M. Robert [a], J.C. Rocha [b], M. van Rijn [c], K. Ahring [d], A. Bélanger-Quintana [e], A. MacDonald [f,*], K. Dokoupil [g], H. Gokmen Ozel [h], A.M. Lammardo [i], P. Goyens [a], F. Feillet [j]

Rocha JC, 2015

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Serum vitamin B_{12} concentrations within reference values do not exclude functional vitamin B_{12} deficiency in PKU patients of various ages

Inge Vugteveen [a,b], Marieke Hoeksma [a,b,*], Anne-Lise Bjorke Monsen [c], M. Rebecca Fokkema [d], Dirk-Jan Reijngoud [b,d], Margreet van Rijn [a], Francjan J. van Spronsen [a,b]

[a] Section of Metabolic Diseases, Beatrix Children's Hospital, University Medical Centre of Groningen, University of Groningen, Groningen, The Netherlands
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[c] Department of Clinical Biochemistry, Haukeland University Hospital, Bergen, Norway
[d] Laboratory of Metabolic Diseases, Department of Laboratory Medicine, University Medical Centre of Groningen, University of Groningen, Groningen, The Netherlands

Importância do doseamento de:

Homocisteína

Ácido Metilmalónico

Rocha JC, 2015

Obrigado pela atenção!