Phenylketonuria - the effects on quality of life and plasma concentrations of phenylalanine and tyrosine of two different amino-acid-suplementations in different concentrations

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of Glycine (258±32 vs 169±44), Alanine (475±65 vs 314±83), Citrulline (80±12 vs 53±12), Arginine (102±14 vs 76±21) and Proline (102±11 vs 59±18) are significantly ($p < 0.05$) higher and these of Taurine (216±62 vs 561±221), Glutamate (13±1 vs 23±15), Valine (137±19 vs 191±38), Isoleucine (47±14 vs 99±21), Leucine (77±19 vs 168±32) and Phenylalanine (58±8 vs 81±12) are significantly ($p < 0.05$) lower. In muscle, concentrations ($nmol.g^{-1}$) of Phenylalanine (95±6 vs 68±21), Lysine (2450±993 vs 710±234), Arginine (855±377 vs 240±100) and Proline (310±32 vs 185±71) are significantly ($p < 0.05$) higher in KO.

Conclusion: Muscle hypertrophy following lack of myostatin modifies the AA pattern. These modifications are mainly focused on gluconeogenic, basic and branched-chain AA. These latter alterations could be related to protein turn-over modifications.

Disclosure of Interest: None declared

PP200

PHENYLKETONURIA – THE EFFECTS ON QUALITY OF LIFE AND PLASMA CONCENTRATIONS OF PHENYLALANINE AND TYROSINE OF TWO DIFFERENT AMINO-ACID-SUPLEMENTATIONS IN DIFFERENT CONCENTRATIONS

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Rationale: Phenyl Keton Urea (PKU) is an inborn error of metabolism. Mental retardation is prevented by early treatment with low protein (LP) diet, supplemented with a phenylalanine (Phe)-free amino acid (AA) mixture. Supplementation of large neutral amino acid (LNAA) and a semi-free (SF) diet has been shown to have a positive effect on well being (1). LNAA has been used as alternative treatment for adult PKU patients in Denmark since 1985. The aim of this study was to investigate the effects of 2 different products, LNAA1* versus LNAA2**, containing LNAA in different combinations, on plasma Phe levels in early treated adults with PKU, as well as the effects on quality of life (QOL).

Methods: Twelve adult PKU patients (6 males, 6 females) entered a double blind, cross over study with four consecutive three-week phases. Ten of the 12 completed all 4 phases. Each phase consisted of LNAA1 or 2, either in low or high dosage. Subjects were instructed to continue their usual SF diet, maintain energy intake and complete a 3-day food record and a SF36 questionaire during each phase. At the end of each phase, plasma AA profile was quantified.

Results: There was no correlation between plasma Phe level and LNAA dosage or type of LNAA supplement. However, 2 patients stated that they felt better when taking LNAA-2 in high dosage.

Conclusion: LNAA 1 & 2 in higher dosage than usual do not lower Phe level in the blood, and do not systematically change QOL-maesurements..

*LNAA1: Prekunil tablets, **LNAA2: Neophe tablets, both manufactured by PreKUlab, Korsør, Denmark, who also sponsored the study together with Merck Serono.

References

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Disclosure of Interest: None declared

PP201

EFFECTS OF ESSENTIAL AMINO ACIDS OR GLUTAMINE PRIVATION ON INTESTINAL PERMEABILITY AND PROTEIN SYNTHESIS: INVOLVEMENT OF MTOR AND GCN2 PATHWAYS

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Rationale: GCN2 and mTOR pathways are involved in the regulation of protein metabolism in response to amino acid availability in different tissues. However regulation at intestinal level is poorly documented. The aim of the study was thus to evaluate the effects of a privation of essential amino acids (EAA) or glutamine (Gln) in intestinal epithelial cells.

Methods: Intestinal epithelial cell, HCT-8, were incubated during 6 hours with (1) DMEM culture medium containing 1% of EAA, 1% of non EAA and 2mM of Gln, (2) PBS as positive control, (3) DMEM without EAA, (4) DMEM without Gln and (5) DMEM without Gln and supplemented with a glutamine synthase inhibitor (MSO, 4 mM). Transepithelial electric resistance (TEER) was measured and fractional synthesis rate (FSR) was assessed by using incorporation of d3-leucine. Expression of eiF2a (phosphorylated or not), used as marker of GCN2 pathway, and of 4E-BP1 (phosphorylated or not), used as a marker of mTOR pathway, was evaluated by immunoblot.

Results: Values (means±SE, n = 6) of TEER and FSR were displayed in table 1. After privation of EAA, TEER and FSR were not significantly affected whereas p-4E-BP1 decreased and p-eiF2a increased. After Gln privation, only FSR and p-4E-BP1 decreased. MSO induced a marked decrease of TEER and FSR and an increase of p-eiF2abut no modification of p-4E-BP1.

Table 1

	(1) control	(2) PBS	(3) EAA−	(4) Gln−	(5) Gln− (+MSO)
TEER (Ohm/H0)	−14±7 (a)	−196±21 (b)	−97±23 (a,c)	−77±35 (a,c)	−136±12 (b,c)
FSR (%/d)	66.7±3.9 (a)	30.9±1.6 (b)	68.4±2.8 (a)	49.8±0.9 (c)	18.0±1.1 (d)

Values without a common letter differ, $p < 0.05$.

Conclusion: These results showed that glutamine depletion decreases more markedly protein synthesis and barrier function than essential amino acid depletion in HCT-8 cells. The effects of glutamine privation are mainly related to an activation of GCN2 pathway.

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