Re-assessment of Phenylalanine Tolerance in Adults with PKU is Needed to Insure Adequate Phenylalanine Intake

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Abstract

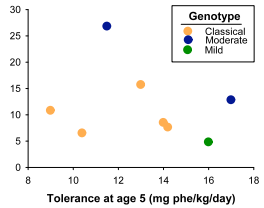
Background: Lifelong treatment of phenylketonuria (PKU) includes a phenylalanine (phe) restricted diet that provides sufficient phe for growth and maintenance plus phe-free amino acid formula to meet requirements for protein, energy and micronutrients. Phe tolerance is the amount of phe those with PKU can consume (mg phe/kg body weight) and maintain acceptable blood phe levels; it requires individual assessment due to varying phenylalanine hydroxylase activity.

Objective: We reassessed phe tolerance in 8 adults with PKU considering genotype, phe tolerance at 5 years of age, phe requirements and blood phe levels.

Method: Subjects completed 3-day food records and collected blood spots that were analyzed for phe with tandem mass spectroscopy. If their blood phe levels were within an agreed-upon acceptable range, phe intake was increased until blood phe levels exceeded the acceptable range. Subjects had not received a personalized evaluation of phe tolerance in 2-18 years, and 5 were currently overweight, BMI 25-28. Tolerance at age 5 was determined based on a chart review, all subjects were genotyped for their expected phenotype[1].

Results: Adult phe tolerance could not be predicted from tolerance at 5 years of age. Only the 5 subjects with a genotype consistent with classical PKU showed the expected phenotype as determined by the Guldberg classification (1). At the start of dietary reassessment 5 subjects were not meeting the mean minimum phe requirement for adults as established by direct amino acid oxidation of phe (9.1 mg phe per kg; (2)). With the guidance of a metabolic dietitian, 3 subjects increased their phe tolerance by 15-33% (+39 to +184 mg phe/day) while 4 subjects increased 79-173% (+241 to +1135 mg phe/day) and 1 decreased 16% (-143 mg phe/day). Subjects significantly increased dietary phe tolerance without significantly increasing blood phe levels. The best single predictor of the extent to which subjects increased their phe tolerance during reassessment was increased frequency of formula consumption (R^2=0.52). Predictors of higher final phe tolerance following reassessment included being male and having a lower BMI.

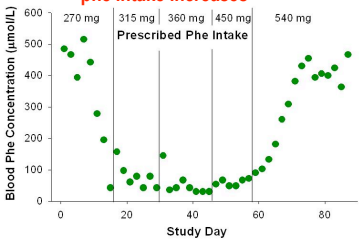
Results



No correlation was found between phe tolerance at age 5 and adult following reassessment, R^2= -0.119, p=0.597.

Results

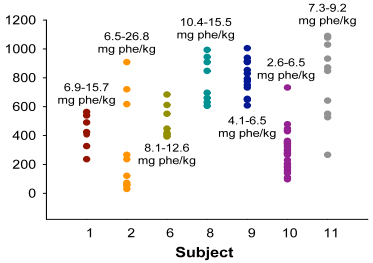
Phe concentrations with biweekly phe intake increases



Subject 7 kept daily food records and good agreement between prescribed and analyzed phe was shown (4.3% ± 25, n=83). This subject doubled her dietary phe intake.

Subjects showed different blood phe concentrations with similar dietary phe intakes (mg phe/kg).

Range of blood phe concentration

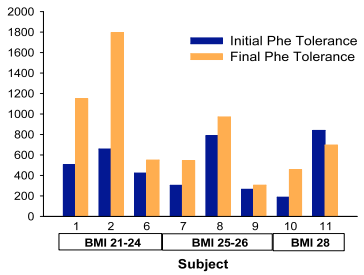


Profile of PKU Subjects and Reassessment of Phe Tolerance

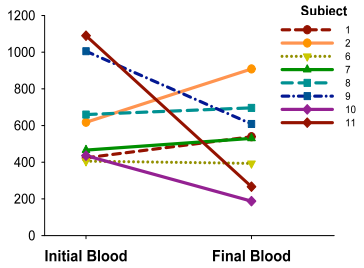
Subject / sex	Age	Expected Phenotype[1]	Tolerance at age 5 (mg/kg)	Initial Tolerance (mg/kg)	Final Tolerance (mg/kg)	Final Tolerance (mg/kg IBW)
1/M	27	Classic	13	6.9	15.7	NA
2/M	29	Moderate	11.5	9.8	26.8	NA
6/F	23	Classic	9	8.1	10.8	NA
7/F	28	Classic	14	4.7	8.5	10.6
8/M	27	Moderate	17	10.4	12.8	14.7
9/F	20	Mild	16	4.1	4.8	6.1
10/F	31	Classic	10.4	2.6	6.5	9.2
11/M	28	Classic	14.2	9.2	7.7	9.3
Mean	27 ± 1		13.1 ± 1	7.0 ± 1	11.7 ± 2.5	10.0 ± 1.4
		Mean Formula Frequency (times/day)		2.2 ± 0.4	3.0 ± 0	

Expected phenotype as classified by Guldberg et al[1]. The minimum phe requirement for healthy adults is 9 mg/kg/day[2]. Five subjects not receiving this minimum at the initial time point. When ideal body weight (IBW) was calculated[3], only one subject was not meeting the minimum requirement by the end of the study.

Drinking formula more frequently was the best single predictor of how much subject increased phe tolerance.



Subjects increased dietary phe intake (paired t-test; p=0.06)



without a significant change in blood phe concentration. (paired t-test; p=0.36)

Predictors for higher final phe tolerance included being male and having a lower BMI.

Conclusion

- Phe tolerance may change with changing body mass. Reassessment in relation to individual body weight and current sensitive measures of phe requirements (9.1 mg phe/kg ideal body weight/ day) is essential to insure adequate phe intake and protein synthesis.
- A metabolic dietitian can guide phe reassessment and help to improve lifelong adherence to the PKU diet and overall health. This process may also allow individuals to review the diet in a positive way by adding more phe, rather than focusing on phe restriction.
- Our results support the need for new guidelines for those with PKU after childhood[3] by showing that periodic reassessment of phe tolerance is essential to optimize diet for life.

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