

Classical treatment versus Tyrosine and Tryptophan supplement in PKU Similar effects on plasma branched chain amino acid levels

*Ingrid Mikkelsen, Kirsten Kiær Abring, Maria Miranda,
Flemming Güttler, Troels Kjær, Hans Lou
Department of Neuropaediatrics,
J.F. Kennedy Institute, Glostrup, Denmark.*

Introduction and background

In adolescence, compliance with conventional PKU treatment is often poor. We have developed a simplified treatment regimen consisting of moderate protein restriction supplemented by essential amino acids without phenylalanine but enriched by tyrosine and tryptophan (PreKUnil).

Here we present data showing the effect of the two treatment regimens on plasma amino acid concentration showing that in spite of threefold increase in phenylalanine intake plasma amino acid concentrations are essentially unchanged.

Patient data

16 patients, 10 males and 6 females, with PKU were followed during a transition from using conventional diet regime consisting of amino acid powder and low protein diet to alternative regime consisting of PreKUnil tablets, containing branched amino acids and high dosages of tyrosine and tryptophan, and semi free diet.

Age was between 15-27 years, mean 17,81 years, weight ranged from 51,5 – 100 kilograms, mean 63,45 kilograms. Purpose of the study was to determine that the amino acid concentration in plasma remained the same despite the change of treatment procedure.

Patient data

Patient	Age	Sex	Weight	Mutation 1	Mutation 2	PKU	Phe. mg/kg BW		
							Conv. diet	Normal	PreKUnil tablets
1	17	M	100	Y414C	IVS1 2nt1 g->a	mild	16	50	+30
2	19	M	72	IVS10 nt-11 g->a	IVS1 2nt1 g->a	severe	14	50	+27
3	15	M	55	IVS10 nt-11 g->a	IVS1 2nt1 g->a	severe	12	50	+24
4	15	M	58	R261Q	R408W	moderate	16	50	+24
5	16	M	57	S349P	R408W	severe	12	50	+27
6	27	M	60	R408W	IVS12nt1g->a	severe	20	50	+24
7	22	M	60	IVS7nt1 g->a	IVS12nt1g->a	moderate	22	50	+24
8	15	M	57	IVS12nt1 g->a	IVS1 2nt1 g->a	severe	13	50	+30
9	18	M	70	R158Q	IVS1 2nt1 g->a	severe	14	50	+24
10	18	M	70	Y356X	IVS1 2nt1 g->a	severe	11	50	+24
11	15	F	52	R408W	IVS1 2nt1 g->a	severe	11	50	+24
12	15	F	58	G46S	IVS1 2nt1 g->a	mild	20	50	+21
13	16	F	74	R408W	R408W	severe	11	50	+27
14	18	F	60	F39L	IVS12nt1g->a	mild	21	50	+21
15	16	F	53	Y414C	IVS1 2nt1 g->a	mild	20	50	+21
16	23	F	63	IVS1 Ont-11 g->a	IVS1 Ont-11 g->a	severe	5	50	+24

Teat meals

Conventional Diet	Normal Diet PreKUnil-tablets
50 g. Albumaid or 30 g. Phenydon or 70 g. Maxamaid or 30 g. Less Taste	60 g. Normal bread 10 g. Butter 10 g. Liver spread
90 g. LP. bread 15 g. Butter 15 g. Normal bread 20 g. Jam 100 g. Fruit 200 ml. PKU milk	5 g. Salami 25 g. Corn flakes 50 ml. Creme
Phe. 118 mg. Protein 19.2g.	Phe. 454 mg. Protein, naturally 9.6 g. tablets 4 g. Protein
KJ. 2545	KJ. 2374

Measurements of all 20 Amino Acid Status in Plasma Serum

20 amino acids were measured in four conditions:

- 1) AA powder and diet, fasting.
- 2) AA powder and diet, 1 hour after a meal.
- 3) PreKUnil and semi free diet, fasting.
- 4) PreKUnil and semi free diet, 1 hour after a meal.

The change from fasting to 1 hour after the two meals differed in only 4 instances: lysine, isoleucine, leucine and alpha-NH₂-n-butamic acid. These amino acids increased significantly (paired T-test) more 1 hour after the meal when on classical treatment. There was no significant difference in tyrosine and tryptophan or phenylalanine changes.

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The change from fasting to 1 hour after the two meals differed in only 4 instances:

Isoleucine, leucine and alpha-NH₂-n-butaric acid.

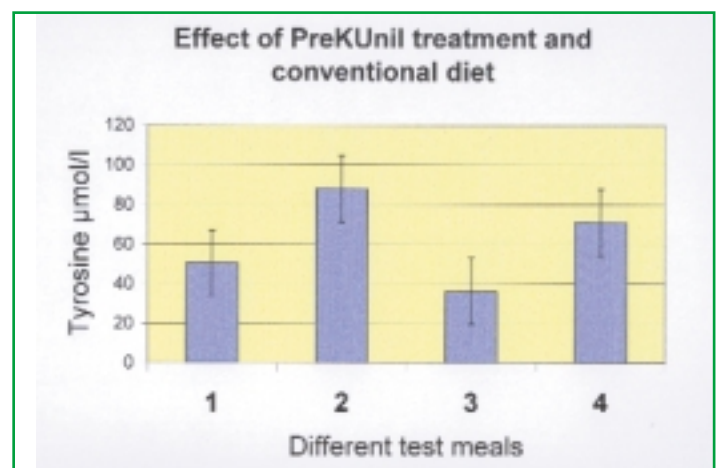
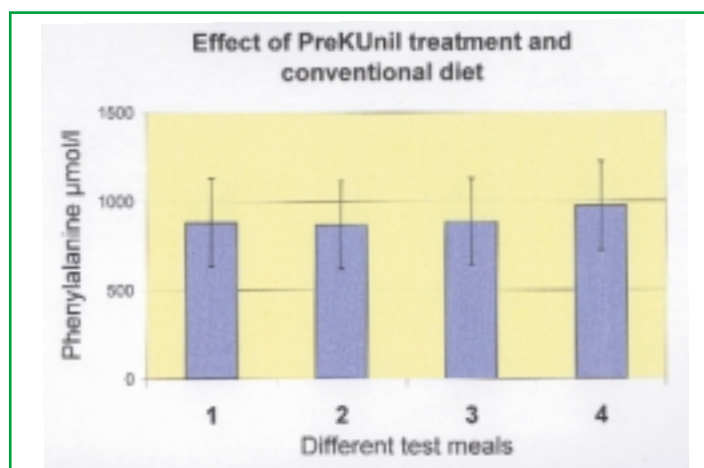
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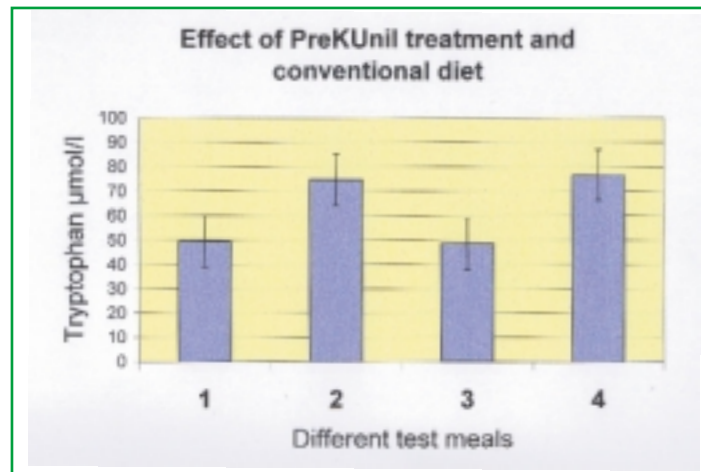
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Plasma Amino acid change (t-test) after meal with Amino acid supplementation

Comparison between conventional and PreKUnil treatment

		Conventional treatment Mean change in AA level/ μ mol	PreKUnil treatment Mean change in AA level/ μ mol
Aspartic acid	N S	2	0
Threonine	N S	55	10
Serine	N S	19	-2
Asparagine	N S	-13	10
Glutamic acid	N S	28	20
Glutamine	N S	39	-4
Proline	N S	82	-2
Glycine	N S	-8	-13
Alanine	N S	114	54
Citrulline	N S	6	0
Amino butyric acid	P = 0,04	3	0
Valine	N S	105	37
Cysteine	N S	2	12
Methionine	N S	11	15
Isoleucine	P = 0,01	49	10
Leucine	P = 0,0008	77	2
Tyrosine	N S	38	35
Phenylalanine	N S	-16	91
Tryptophan	NS	25	28
Ornithine	N S	-4	-3
Lysine	P = 0,0022	73	-16
Histidine	N S	11	10
Arginine	N S	35	20





Discussion

The purpose of the study was to determine whether there is an alteration in the amino acid profile in the comparison of conventional therapy and alternative treatment with PreKUnil.

Compliance among young adults with PKU has not been good on conventional diet, which has been the main reason for introducing this alternative treatment.

Conclusion

Measurements of amino acid profiles shows, that there is no significant difference in branched chain amino acid levels after a con-

ventional PKU therapy meal and alternative treatment with semi-free meal and PreKUnil supplementation.