

Laron Syndrome Patients Have an Abnormal Plasma Amino Acid Pattern, Reversed by IGF-I Treatment

Barazani Chen PhD¹, Laron Zvi MD PhD(hc)²

¹Metabolic laboratory, ²Endocrinology and Diabetes Research Unit, Schneider Children's Medical Center, Petah Tikva. Sackler Faculty of Medicine, Tel Aviv University, Israel.

1 Background

Laron Syndrome (LS), (OMIM#262500) is rare recessively inherited disease caused by deletions or mutations of the GH receptor, and characterized by low or undetectable serum IGF-I(1). This deficiency leads to a series of metabolic abnormalities including of the proteins. Due to long standing IGF-I deficiency there is general underdevelopment of the muscular system composition reduced muscular mass(2,3), force and endurance(4).

2 Aim of Study

To define the differences of Amino Acids plasma composition in Laron Syndrome patients with and without IGF-I treatment compare with control group.

3 Subjects

We studied 3 untreated and, 2 IGF-I treated LS patients, 2 heterozygote mothers, 1 healthy brother, 2 young females (one of treated Turner syndrome & one of early PCOS) and 3 aged subjects.

4 Methods

Plasma Amino analysis was performed using the Waters solvent delivery system (Acquity UPLC H-Class + Waters Xevo TQ-S micro Tandem mass). Chromatographic separation was achieved by using Waters Cortecs C-18 column. Quantitative values were obtained by relating chromatographic peak areas to those derived from calibration curves.

Table 1: Clinical details: patients sex, age and serum IGF-I levels.

S/N	Subjects	Sex	Age	IGF-I ug/kg/d	IGF-I ng/ml
1.a	LS Homozygote	M	10	106	43
1.b	LS Homozygote	M	11	150	61
2	LS Homozygote	F	17	148	275
3	LS Homozygote	F	58	-	26
4	LS Homozygote	F	29	-	<15
5	LS Homozygote	M	42	-	47
6	LS Heterozygote	F	45	-	155
7	LS Heterozygote	F	38	-	148
8	Old age	F	87	-	107
9	Old age	F	89	-	133
10	Old age	M	91	-	93
11	Turner S.	F	18	-	322
12	PCOS	F	17	-	403
13	Healthy	M	5	-	107

5 Results

In the first report we shows the long term IGF-I deficiency in LS, causes changes in the plasma amino acids composition. The main findings are summarized in table 2.

Plasma Citruline and Sarcosine were low in the untreated LS patients and decrease upon IGF-I administrations, so did α-aminoadipic acid. Taurine levels were low in untreated LS patients, heterozygotes and old subjects. IGF-r treatment normalized the values.

Serum total proteins and albumin were normal in all subjects tested. The untreated LS patients have increased plasma Sarcosine levels which increased further during IGF-I treatment This is the first report that shows the long term IGF-I deficiency in LS, causes change in the plasma amino acids composition.

Table 2: Plasma amino acids in LS patients and control groups as mean +/- SD per group.

Pt. Group	Sar umol/l	Cit umol/l	a-AADA umol/l
1. LS+	1.7	20	↑ 2.7
2. LS-	↑ 1	↓ 11.6	1.4
3. Htro.	↑ 0.1	↓ 7.1	1.1
4. O.A.	↑ 0.7	23.9	2.3
5. Endo	0.5	8.3	↑ 2
6. Ctrl.	1.3	13.1	1

Legend: LS+: IGF-I treatment, LS-: No treatment, Htro: Hetrozygote, O.A.: Old aged, Endo: Endocrine disease, Ctrl.: Healthy control.

Reference Values		
Amino Acid	25mo-18Y	>=19Y
Cit=Citruline	1.0-46	12.0-55
a-aminoadipic acid	0	0-6
Sar=Sarcosine	0-9	0

6 Conclusions

1. Congenital IGF-I deficiency alters the plasma amino acid composition changes which are partial reversible by long term IGF-I therapy.
2. Comparison with AA changes in old age with markedly reduced IGF-I levels.

7 References

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