MOLECULAR INVESTIGATION OF GLUTARIC ACIDURIA TYPE1 IN IRAN

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Glutaric Acidemia, Type I (GA I), was first described in 1975. The disease is caused by a genetic deficiency of the enzyme, Glutaryl-CoA Dehydrogenase (GCD), which leads to the buildup of Glutaric acid in the tissues and its excretion in the urine of affected patients. GCD is involved in the catabolism of the amino acids, Lysine, Hydroxylysine, and Tryptophan. Over 200 cases of GA I have been reported in the medical literature. GA I is one of the most common organic acidemias and has an estimated incidence of about 1 in 50,000 live births.

Because of the initial slow progression of clinical symptoms, GA I is frequently undiagnosed until an acute metabolic crisis occurs. A total of 25 unrelated patients suspected to GA1 were investigated in our study. Genomic DNA was extracted from peripheral blood cells of the 25 probands whom were biochemically and/or clinically and/or neuro-radiologically suspected to GA1. 15 of them had elevated glutaric acid in the urine organic acid test.

PCR and direct sequencing of all 11 exons and their flanking region of the GCDH gene were examined.Some of them were investigated for known mutation in the other their family members. Fifteen patients had homozygous mutations and 10 patients were normal for GCDH gene. Our Results Showed:

- 60% Known mutation were found in our 15 patients
- 80% can be detected by 4 exons sequencing so for molecular investigatins exon 6, 7, 8, 10 are good choice for beginning of analysis
- 33% was mutation in exon 7, so because of the cost of genetic diagnosis we suggest that investigation begin with this exon.
- Pro 348 Leu was most detected 20%.
- 40% are new mutations wich will be investigated for phenotype Genotype Correlations

Keywords: Glutaric Aciduria; Iranian population;Mutation detection.

Table: Mutation Detection on Glutaric Aciduria ‘s gene in Iranian patients

No.	Nucleotide substitution		Aminoacid change	Codon no.	Exon	Number of patients	Type of report	Reference
1	T>C	CTC>CCC	Leu>Pro	179	6	1	unreported	
2	G>C	GAG>CAG	Glu>Gln	181	6	2	reported	Zschocke (2000) J Med Genet 37, 177
3	T>C	TTC>CTC	Phe>Leu	236	7	1	reported	Goodman (1998) Hum Mutat 12, 141
4	G>T	GGT>TGT	Gly>Cys	244	7	1	unreported	
5	C>T	CCC>CTC	Pro>Leu	248	7	3	reported	Zschocke (2000) J Med Genet 37, 177
6	G>C	CGG>CCG	Arg>Pro	294	8	1	unreported	
7	G>A	CGG>CAG	Arg>Gln	294	8	1	unreported	
8	C>T	CTT>TTT	Leu>Phe	302	8	1	unreported	
9	A>G	AAT>AGT	Asn>Ser	373	10	1	unreported	
10	G>A	CGG>CAG	Arg>Gln	402	10	1	reported	Goodman (1998) Hum Mutat 12, 141
11	C>T	ACG>ATG	Thr>Met	429	11	1	reported	Schwartz (1998) Hum Genet 102, 452
12	C>T	GCG>GTG	Ala>Val	433	11	1	reported	Busquets (2000) Pediatr Res 48, 315