P-187 - GENOTYPE AND PHENOTYPE CORRELATION IN CHILEAN PKU PATIENTS

Hamilton V¹, Santa María L¹, Fuenzalida K¹, Morales P¹, Desviat LR², Ugarte M², Pérez B², Castro-Chaves G¹, Cabello JF¹, Cornejo V¹

(1) Instituto de Nutrición y Tecnología de los Alimentos, Dr. Fernando Monckeberg Barros, Universidad de Chile. Santiago – Chile. (2) Centro de Diagnóstico de Enfermedades Moleculares (CEDEM), CIBERER Universidad Autónoma de Madrid, Spain. vhamilton@inta.uchile.cl.

INTRODUCTION: Phenylketonuria (PKU, OMIM 261600) is an autosomal recessive disease, caused by mutations in the Phenylalanine Hydroxylase (PAH) gene situated in chromosome 12q22-q24.2. The genotype is one of the main factors that determine the phenotype of this disease. OBJECTIVE: Correlate genotype and phenotype in Chilean PKU patients. METHODS: We classified the phenotype according to: phenylalanine (Phe) levels at diagnosis, phenylalanine tolerance at 1 and 5 years old in 57 PKU subjects. Then correlate the genotype (by Guldberg predicted value) with those phenotypes. Fisher exact test was used. Significance level was set at p<0.05. Statistical analysis was performed using STATA 13. RESULTS: We identified 26 different mutations in 134 of the 142 alleles studied (94.4%), 88.7% of the subjects had biallelic pathogenic mutations. Compound heterozygous represented 85.9% of the cases. Exon 7 included the majority of mutations (26.9%) and 50% of mutations were missense. The most frequent mutations were c.1066-11G>A, c.442-?_509+?del and p.Val388Met. The majority of subjects (52.3%) had the classic phenotype. The sample with biallelic mutations (n=57) diagnosis Phe levels were 1092±480 umol/L at 17.2±10 days of age. Phe intake in the first year of life was 39.8±8.5 mg/kg/d and 23.3±14.2 mg/kg/d at age 5. There was a correlation between genotype and phenotype according to Phe levels at diagnosis and with Phe tolerance at 1 year of age (p=0.02 and p=0.005, respectively). According to genotype only 14% could respond to BH4. Our most frequent mutation (p.Val388Met) has the highest discrepancy between genotype and phenotype. CONCLUSIONS: Genotype characterization allowed us to predict the phenotype in our Chilean patients only during the first year of life (phe levels at diagnosis and tolerance). There is no concordance between genotype and phenotype in older patients. It is important to mention that cases with the p.Val388Met mutation have a more severe phenotype than described in literature.