P-174 - GENOTYPE-PHENOTYPE CORRELATION IN BRAZILIAN PATIENTS WITH CLINICAL DIAGNOSIS OF CLASSICAL HOMOCYSTINURIA

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Classical homocystinuria (HCU) is an autosomal recessive inborn error of metabolism, caused by a deficiency of the enzyme cystathionine β-synthase (CBS). This deficiency results in the elevated plasma levels of homocysteine and methionine and the most common clinical manifestations are dislocation of optic lens, mental retardation, skeletal deformities, and thromboembolism. The correlation between disease severity and genotype is still not well established. The aim of this study was to correlate genotype with phenotype in 22 Brazilian patients (19 families) with the clinical diagnosis of HCU. **RESULTS:** The molecular analysis revealed eight known pathogenic mutations in the CBS gene described as causing HCU and two novel mutations non-pyridoxine responsive (G351R and L364V). All presented variations were classified according to ACMG guidelines and for the frequency of variants in the Brazilian population the Online Archive of Brazilian Mutations (ABraOM) was used. The most frequent mutation in our sample was G151R (seven patients). The phenotype was classified as severe (B6 non-responsive) and mild (B6-responsive). Patients who developed any new VTE and worsening of lens dislocations were classified in bad prognosis group (BPG), all the others were classified in good prognosis group (GPG). We used the software Prism 5.0, Graph Pad (San Diego, CA) and Mann-Whitney test to assess whether the difference in tHcy levels between two groups (GPG/BGP) was significant (p <0.05). The patients on GPG presented the median tHcy level of 42±4 µmol/L (n=13) and patients on BPG, the median of 181±70 µmol/L (n=7) for years in treatment. The genotype-phenotype correlation for known mutations I278T, G151R, T353M, T191M, W323*, E302K, R379W, and R266K is in accordance with the literature. Gathering our data to all reports in the Brazilian population, G151R becomes the most frequent allele (n=20), followed by I278T (n=19), T191M (n=16) and W323* (n=14). **CONCLUSION:** In summary, considering these findings, we characterized molecularly and clinically Brazilian patients with a late diagnosis of HCU and contributed to the disease genotype-phenotype classification with clinical outcome of years in classical HCU treatment.