P-006 - HEREDITARY FRUCTOSE INTOLERANCE: NGS APPROACH TO IMPROVE AND CONFIRM THE GENETIC DIAGNOSIS OF BRAZILIAN PATIENTS

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INTRODUCTION: The ALDOB gene comprises 9 exons and encodes the aldolase B (E.C.4.1.2.13), a key enzyme in energetic pathways as glycolysis, glycogenesis, and gluconeogenesis. Individuals with aldolase B deficiency (hereditary fructose intolerance – HFI), an inborn error of fructose metabolism, present hypoglycemia after fructose intake, liver dysfunction and mild hepatomegaly. The analysis of the ALDOB sequence has been used to perform the diagnosis of this disorder.

AIMS: To analyze the ALDOB gene in Brazilian patients with clinical suspicion of HFI.

MATERIALS AND METHODS: Fifteen unrelated patients were analyzed by NGS in IonTorrent PGM platform (Life Technologies) with a customized panel including the exonic regions and the intron-exon boundaries of ALDOB gene. The minimal coverage was 200X. The variants found were confirmed by automated Sanger sequencing. Patients with no mutations detected by NGS were also analyzed by Sanger. The haplotype analysis was performed with LDlink suite and data of populations from 1000 Genomes project.

RESULTS: Six patients had the diagnosis of HFI confirmed (from South region: 5; from Minas Gerais-MG: 1). Three different mutations were identified: c.448G>C in exon 5 (n=6 alleles, all from the South), 360_363delCAAA in exon 4 (n=4; South=3, MG=1) and 178C>T in exon 3 (n=2; South=1, MG=1). The analyses demonstrated that c.178C>T and c.360_363delCAAA mutations present two different haplotypes each: one haplotype was present in patients from MG and other in patients from the South. In nine patients, no mutations were detected after NGS and Sanger sequencing.

CONCLUSION/DISCUSSION: The genetic profile of the patients in this study is similar to the one observed in a study including patients from other American countries (USA, Canada, Argentina). However, the frequency of mutations is different from that found in a previous study with Brazilian patients from MG in which the mutation c.448G>C was the less frequent allele found. We suggest a targeted analysis in ALDOB to detect the c.178C>T, 360_363delCAAA and c.448G>C mutations as an approach to perform the diagnosis of HIF in Brazil.